

ANEXO 1

Análisis estadístico del desempeño del ELISA basado en NS1 para detectar IgM DENV específica circulante usando como estándar de oro el estuche comercial Standard Diagnostics INC. Panbio Arele Dengue IgM Capture ELISA, Ref: 01PE20. Gyeonggi-do, Korea.

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Frequencies of Agreement

Category	Maximum Possible	Chance Expected	Observed
1	203	127.81	197
2	130	54.81	124
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7			
8			
Total	333	182.62	321

IgM DENV NS1

Estándar de oro: Estuche de Panbio-Arele

Proportions of Agreement

Category	Maximum Possible	Chance Expected	Observed	.95 CI of Observed	
				Lower Limit	Upper Limit
1	0.9186	0.4315	0.8678	0.8151	0.9077
2	0.8784	0.2456	0.8052	0.732	0.8628
3	---	---	---	---	---
4	---	---	---	---	---
5	---	---	---	---	---
6	---	---	---	---	---
7					
8					
Composite	0.9487	0.5203	0.9145	0.879	0.9407

Confidence intervals for proportions are calculated according to the Wilson efficient-score method, corrected for continuity.

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Data Entry

		B								
		1	2	3	4	5	6	7	8	Totals
A	1	197	6	----	----	----	----	----	----	203
	2	24	124	----	----	----	----	----	----	148
	3	----	----	----	----	----	----	----	----	----
	4	----	----	----	----	----	----	----	----	----
	5	----	----	----	----	----	----	----	----	----
	6	----	----	----	----	----	----	----	----	----
	7	----	----	----	----	----	----	----	----	----
	8	----	----	----	----	----	----	----	----	----
Totals		221	130	----	----	----	----	----	----	351

The designation "nc" appearing in any of the following cells means "this quantity cannot be calculated." This will typically occur only when your data entries in the above table include a substantial proportion of zeros.

Unweighted Kappa

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.8218			
Method 1	0.0311	0.7608	0.8828
Method 2	0.0309	0.7612	0.8824

maximum possible unweighted kappa, given the observed marginal frequencies
 observed as proportion of maximum possible

Kappa with Linear Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.8218	0.0309	0.7612	0.8824

maximum possible linear-weighted kappa, given the observed marginal frequencies
 observed as proportion of maximum possible

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	Condition		Totals
	Absent	Present	
Test Positive	6	197	203
Test Negative	124	24	148
Totals	130	221	351

Calculate

Reset

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.62963	0.576514	0.67986
Sensitivity	0.891403	0.840919	0.92779
Specificity	0.953846	0.897967	0.9811
For any particular test result, the probability that it will be:			
Positive	0.578348	0.524679	0.630273
Negative	0.421652	0.369727	0.475321
For any particular positive test result, the probability that it is:			
True Positive (Positive Predictive Value)	0.970443	0.933771	0.987929
False Positive	0.029557	0.012071	0.066229
For any particular negative test result, the probability that it is:			
True Negative (Negative Predictive Value)	0.837838	0.766279	0.891352
False Negative	0.162162	0.108648	0.233721
Likelihood Ratios:			
[C] = conventional			
[W] = weighted by prevalence [definitions]			
Positive [C]	19.313725	8.828588	42.251376
Negative [C]	0.113852	0.077979	0.166227
Positive [W]	32.833333	14.92208	72.2438
Negative [W]	0.193548	0.133856	0.279861
The entry 'NaN' in any of the above cells means that the calculation cannot be performed because the values entered include one or more instances of zero. Technical note on calculation of confidence intervals.			

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ANEXO 2

Análisis estadístico del desempeño del ELISA basado en NS1 para detectar IgM-DENV específica circulante usando como estándar de oro el estuche comercial Anti-Dengue Virus ELISA (IgM), ref: El 266b-9601 M, Lot: E211202CA, EUROIMMUN, Medizinische Labordiagnostika AG, Germany, IVD, RI 2017RD-0004083.

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Kappa with Quadratic Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.3459	0.0345	0.2783	0.4135

IgM DENV NS1

Estándar de oro: Estuche EUROIMMUN IgM

0.4179	maximum possible quadratic-weighted kappa, given the observed marginal frequencies
0.8277	observed as proportion of maximum possible

Frequencies of Agreement

Category	Maximum Possible	Chance Expected	Observed
1	74	39.18	68
2	152	117.18	146
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7			
8			
Total	226	156.36	214

Proportions of Agreement

Category	Maximum Possible	Chance Expected	Observed	.95 CI of Observed	
				Lower Limit	Upper Limit
1	0.4327	0.1903	0.3842	0.313	0.4604
2	0.6104	0.4128	0.5725	0.5092	0.6336
3	---	---	---	---	---
4	---	---	---	---	---
5	---	---	---	---	---
6	---	---	---	---	---
7					
8					
Composite	0.6997	0.4841	0.6625	0.6077	0.7134

Confidence intervals for proportions are calculated according to the Wilson efficient-score method, corrected for continuity.

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Data Entry

		B								Totals
		1	2	3	4	5	6	7	8	
A	1	68	103	----	----	----	----	----	----	171
	2	6	146	----	----	----	----	----	----	152
	3	----	----	----	----	----	----	----	----	----
	4	----	----	----	----	----	----	----	----	----
	5	----	----	----	----	----	----	----	----	----
	6	----	----	----	----	----	----	----	----	----
	7	----	----	----	----	----	----	----	----	----
	8	----	----	----	----	----	----	----	----	----
Totals		74	249	----	----	----	----	----	----	323

Reset

Calculate

The designation "nc" appearing in any of the following cells means "this quantity cannot be calculated." This will typically occur only when your data entries in the above table include a substantial proportion of zeros.

Unweighted Kappa

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.3459			
<u>Method 1</u>	0.051	0.246	0.4458
<u>Method 2</u>	0.0416	0.2644	0.4274

0.4179

maximum possible unweighted kappa, given the observed marginal frequencies

0.8277

observed as proportion of maximum possible

Kappa with Linear Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.3459	0.0416	0.2644	0.4274

0.4179

maximum possible linear-weighted kappa, given the observed marginal frequencies

0.8277

observed as proportion of maximum possible

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	Condition		Totals
	Absent	Present	
Test Positive	103	68	171
Test Negative	136	6	142
Totals	239	74	313

Calculate

Reset

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.236422	0.191254	0.288196
Sensitivity	0.918919	0.825733	0.966609
Specificity	0.569038	0.503558	0.632261

For any particular test result, the probability that it will be:

Positive	0.546326	0.489349	0.602147
Negative	0.453674	0.397853	0.510651

For any particular positive test result, the probability that it is:

True Positive (Positive Predictive Value)	0.397661	0.324561	0.475435
False Positive	0.602339	0.524565	0.675439

For any particular negative test result, the probability that it is:

True Negative (Negative Predictive Value)	0.957746	0.906294	0.982708
False Negative	0.042254	0.017292	0.093706

likelihood Ratios:

[C] = conventional

[W] = weighted by prevalence [\[definitions\]](#)

Positive [C]	2.132249	1.815833	2.503802
Negative [C]	0.142488	0.065761	0.308739
Positive [W]	0.660194	0.529268	0.823508
Negative [W]	0.044118	0.02015	0.096595

The entry 'NaN' in any of the above cells means that the calculation cannot be performed because the values entered include one or more instances of zero.

[Technical note](#) on calculation of confidence intervals.

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ANEXO 3

Análisis estadístico del desempeño del ELISA basado en NS1 para detectar IgM-DENV específica circulante usando como estándar de oro el estuche comercial Virion Serion Classic Dengue virus ELISA IgM, Ref: ESR114M, lote: EL0141, IVD RI: 2017RD-0004405.

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Frequencies of Agreement

Category	Maximum Possible	Chance Expected	Observed
1	64	32.73	57
2	64	32.73	57
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7			
8			
Total	128	65.46	114

IgM DENV NS1

Estándar de oro: Estuche Virion-Serion IgM ELISA

Proportions of Agreement

Category	Maximum Possible	Chance Expected	Observed	.95 CI of Observed	
				Lower Limit	Upper Limit
1	0.9552	0.3331	0.7703	0.6552	0.8568
2	0.9552	0.3331	0.7703	0.6552	0.8568
3	---	---	---	---	---
4	---	---	---	---	---
5	---	---	---	---	---
6	---	---	---	---	---
7					
8					
Composite	0.9771	0.4997	0.8702	0.7976	0.9204

Confidence intervals for proportions are calculated according to the Wilson efficient-score method, corrected for continuity.

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Data Entry

		B								Totals
		1	2	3	4	5	6	7	8	
A	1	57	10	----	----	----	----	----	----	67
	2	7	57	----	----	----	----	----	----	64
	3	----	----	----	----	----	----	----	----	----
	4	----	----	----	----	----	----	----	----	----
	5	----	----	----	----	----	----	----	----	----
	6	----	----	----	----	----	----	----	----	----
	7	----	----	----	----	----	----	----	----	----
	8	----	----	----	----	----	----	----	----	----
Totals		64	67	----	----	----	----	----	----	131

Reset

Calculate

The designation "nc" appearing in any of the following cells means "this quantity cannot be calculated." This will typically occur only when your data entries in the above table include a substantial proportion of zeros.

Unweighted Kappa

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.7406			
<u>Method 1</u>	0.0587	0.6256	0.8556
<u>Method 2</u>	0.0586	0.6257	0.8555

0.9542 maximum possible unweighted kappa, given the observed marginal frequencies

0.7761 observed as proportion of maximum possible

Kappa with Linear Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.7406	0.0586	0.6257	0.8555

0.9542 maximum possible linear-weighted kappa, given the observed marginal frequencies

0.7761 observed as proportion of maximum possible

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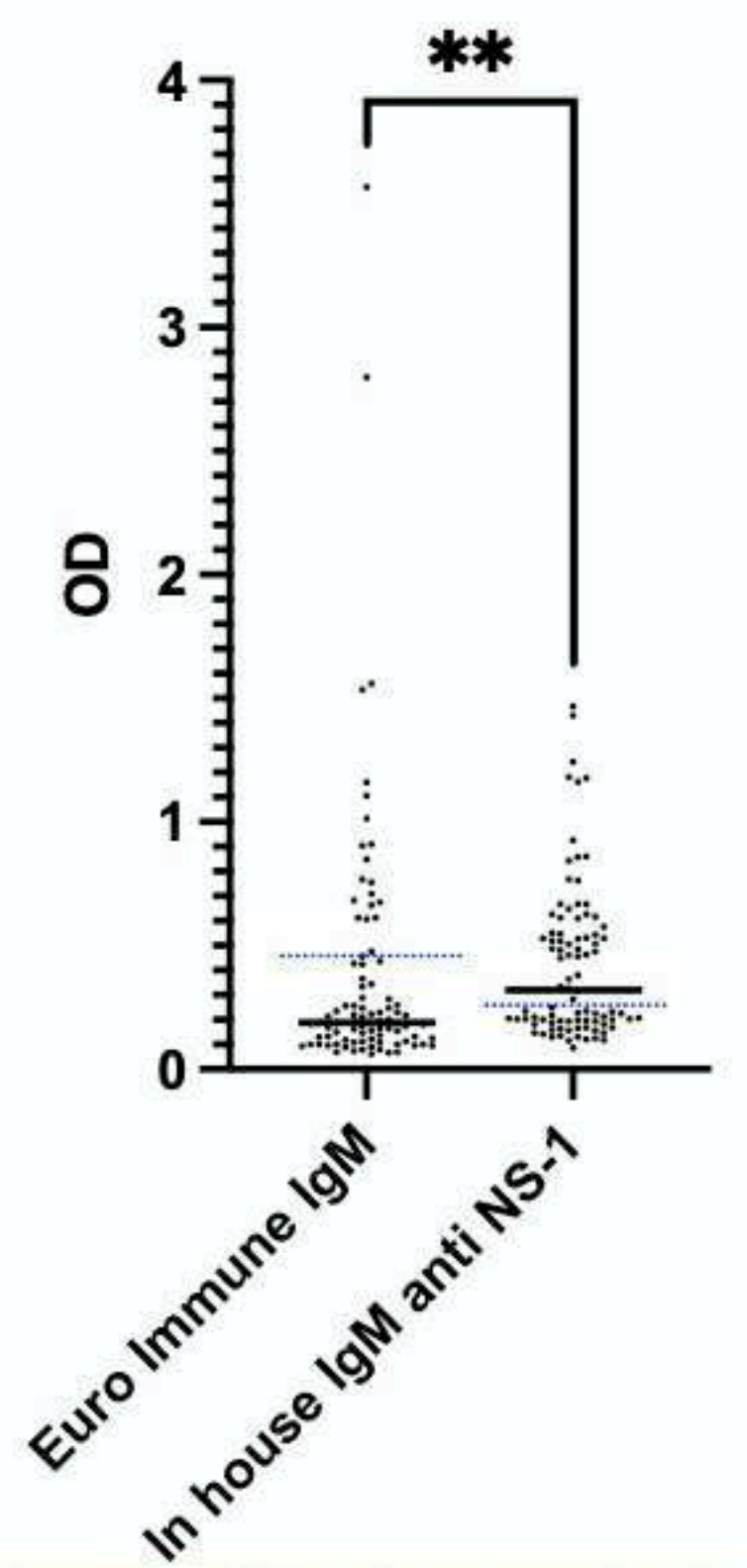
	Condition		Totals
	Absent	Present	
Test Positive	10	57	67
Test Negative	57	7	64
Totals	67	64	131

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.48855	0.400813	0.576967
Sensitivity	0.890625	0.781588	0.951214
Specificity	0.850746	0.737992	0.922306
For any particular test result, the probability that it will be:			
Positive	0.51145	0.423033	0.599187
Negative	0.48855	0.400813	0.576967
For any particular positive test result, the probability that it is:			
True Positive (Positive Predictive Value)	0.850746	0.737992	0.922306
False Positive	0.149254	0.077694	0.262008
For any particular negative test result, the probability that it is:			
True Negative (Negative Predictive Value)	0.890625	0.781588	0.951214
False Negative	0.109375	0.048786	0.218412
likelihood Ratios: [C] = conventional [W] = weighted by prevalence [definitions]			
Positive [C]	5.967188	3.347428	10.63722
Negative [C]	0.128564	0.063573	0.259996
Positive [W]	5.7	3.190134	10.184527
Negative [W]	0.122807	0.060809	0.248014
The entry 'NaN' in any of the above cells means that the calculation cannot be performed because the values entered include one or more instances of zero. Technical note on calculation of confidence intervals.			

ANEXO 4

Reunión con la empresa Byo Colombia S.A.S. en donde se analizaron los resultados obtenidos con el estuche comercial el Anti-Dengue Virus ELISA (IgM), ref: EI 266b-9601 M, Lot: E211202CA, EUROIMMUN. En conclusión, los resultados fueron escalados a casa matriz.

Positive IgM- anti DEN



Reunión | Microsoft Teams

teams.microsoft.com/_#/pre-join-calling/19:meeting_MDE1NzU3MDQTYzAxZC00NTIxLTk1YmEtNjE3NTE0MWFmOTQy@thread.v2

28:15

Byocolombia1

INFORMES TÉCNICOS

MERO

2022-0

This block contains a screenshot of a Microsoft Teams meeting interface. At the top, the browser tabs show '(1) WhatsApp' and 'Reunión | Microsoft Teams'. The address bar displays the meeting URL. The main area shows two video feeds of participants. At the bottom, a control bar includes a timer at 28:15, icons for video, microphone, chat, and a red call button. The name 'Byocolombia1' is visible in the bottom left. On the right side, there are partial views of other windows, including one titled 'INFORMES TÉCNICOS' and another with 'MERO' and '2022-0'.

ANEXO 5

Análisis estadístico del desempeño del ELISA para detectar IgG-DENV basado en NS1, usando como estándar de oro el estuche comercial Panbio-Arele Dengue virus IgG capture ELISA, Standard Diagnostic.

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Kappa with Quadratic Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.7353	0.0323	0.6719	0.7987

IgG DENV NS1

Estándar de oro: Estuche Panbio-Arele.

1	maximum possible quadratic-weighted kappa, given the observed marginal frequencies
0.7353	observed as proportion of maximum possible

Frequencies of Agreement

Category	Maximum Possible	Chance Expected	Observed
1	167	91.44	147
2	138	62.44	118
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7			
8			
Total	305	153.88	265

Proportions of Agreement

Category	Maximum Possible	Chance Expected	Observed	.95 CI of Observed	
				Lower Limit	Upper Limit
1	1	0.377	0.7861	0.719	0.8412
2	1	0.2924	0.7468	0.6704	0.811
3	---	---	---	---	---
4	---	---	---	---	---
5	---	---	---	---	---
6	---	---	---	---	---
7					
8					
Composite	1	0.5045	0.8689	0.8245	0.9036

Confidence intervals for proportions are calculated according to the Wilson efficient-score method, corrected for continuity.

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Data Entry

		B								Totals
		1	2	3	4	5	6	7	8	
A	1	147	20	----	----	----	----	----	----	167
	2	20	118	----	----	----	----	----	----	138
	3	----	----	----	----	----	----	----	----	----
	4	----	----	----	----	----	----	----	----	----
	5	----	----	----	----	----	----	----	----	----
	6	----	----	----	----	----	----	----	----	----
	7	----	----	----	----	----	----	----	----	----
	8	----	----	----	----	----	----	----	----	----
Totals		167	138	----	----	----	----	----	----	305

The designation "nc" appearing in any of the following cells means "this quantity cannot be calculated." This will typically occur only when your data entries in the above table include a substantial proportion of zeros.

Unweighted Kappa

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.7353			
<u>Method 1</u>	0.039	0.6588	0.8118
<u>Method 2</u>	0.039	0.6589	0.8117

maximum possible unweighted kappa, given the observed marginal frequencies

observed as proportion of maximum possible

Kappa with Linear Weighting

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.7353	0.039	0.6589	0.8117

maximum possible linear-weighted kappa, given the observed marginal frequencies

observed as proportion of maximum possible

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	Condition		Totals
	Absent	Present	
Test Positive	20	147	167
Test Negative	118	20	138
Totals	138	167	305

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.547541	0.4898	0.604065
Sensitivity	0.88024	0.81883	0.923537
Specificity	0.855072	0.782634	0.907123
For any particular test result, the probability that it will be:			
Positive	0.547541	0.4898	0.604065
Negative	0.452459	0.395935	0.5102
For any particular positive test result, the probability that it is:			
True Positive (Positive Predictive Value)	0.88024	0.81883	0.923537
False Positive	0.11976	0.076463	0.18117
For any particular negative test result, the probability that it is:			
True Negative (Negative Predictive Value)	0.855072	0.782634	0.907123
False Negative	0.144928	0.092877	0.217366
likelihood Ratios: [C] = conventional [W] = weighted by prevalence [definitions]			
Positive [C]	6.073653	4.034399	9.143682
Negative [C]	0.140059	0.092617	0.211802
Positive [W]	7.35	4.853652	11.130278
Negative [W]	0.169492	0.112746	0.254798
The entry 'NaN' in any of the above cells means that the calculation cannot be performed because the values entered include one or more instances of zero. Technical note on calculation of confidence intervals.			

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ANEXO 6

Análisis estadístico del desempeño del ELISA para detectar IgG-DENV basado en NS1, usando como estándar de oro el estuche comercial El estuche usado fue el Anti-Dengue Virus ELISA (IgG), EUROIMMUN, ref: EI 266b-9601 G, lote: E220128AZ, IVD, RI: 2017RD-0004081-R.

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Frequencies of Agreement

Category	Maximum Possible	Chance Expected	Observed
1	150	101.7	145
2	85	36.7	80
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7			
8			
Total	235	138.4	225

IgG DENV NS1

Estándar de oro: Estuche EUROIMMUN ELISA IgG.

Proportions of Agreement

Category	Maximum Possible	Chance Expected	Observed	.95 CI of Observed	
				Lower Limit	Upper Limit
1	0.838	0.4475	0.788	0.7205	0.8433
2	0.7456	0.2262	0.6723	0.5794	0.7539
3	---	---	---	---	---
4	---	---	---	---	---
5	---	---	---	---	---
6	---	---	---	---	---
7					
8					
Composite	0.8902	0.5242	0.8523	0.8023	0.8917

Confidence intervals for proportions are calculated according to the Wilson efficient-score method, corrected for continuity.

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Data Entry

		B								Totals
		1	2	3	4	5	6	7	8	
A	1	145	5	----	----	----	----	----	----	150
	2	34	80	----	----	----	----	----	----	114
	3	----	----	----	----	----	----	----	----	----
	4	----	----	----	----	----	----	----	----	----
	5	----	----	----	----	----	----	----	----	----
	6	----	----	----	----	----	----	----	----	----
	7	----	----	----	----	----	----	----	----	----
	8	----	----	----	----	----	----	----	----	----
Totals		179	85	----	----	----	----	----	----	264

Reset

Calculate

The designation "nc" appearing in any of the following cells means "this quantity cannot be calculated." This will typically occur only when your data entries in the above table include a substantial proportion of zeros.

Unweighted Kappa

Observed Kappa	Standard Error	.95 Confidence Interval	
		Lower Limit	Upper Limit
0.6895			
<u>Method 1</u>	0.0459	0.5995	0.7795
<u>Method 2</u>	0.0446	0.6021	0.7769

0.7691

maximum possible unweighted kappa, given the observed marginal frequencies

0.8965

observed as proportion of maximum possible

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- Correlation & Regression
- t-Tests & Procedures
- ANOVA
- ANCOVA
- Miscellanea
- HOME

	Condition		Totals
	Absent	Present	
Test Positive	5	145	150
Test Negative	80	34	114
Totals	85	179	264

Calculate

Reset

	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.67803	0.617512	0.733272
Sensitivity	0.810056	0.74327	0.863191
Specificity	0.941176	0.861965	0.978143

For any particular test result, the probability that it will be:

Positive	0.568182	0.505979	0.628368
Negative	0.431818	0.371632	0.494021

For any particular positive test result, the probability that it is:

True Positive (Positive Predictive Value)	0.966667	0.919891	0.987664
False Positive	0.033333	0.012336	0.080109

For any particular negative test result, the probability that it is:

True Negative (Negative Predictive Value)	0.701754	0.607741	0.78194
False Negative	0.298246	0.21806	0.392259

Likelihood Ratios:

[C] = conventional

[W] = weighted by prevalence [\[definitions\]](#)

Positive [C]	13.77095	5.866496	32.32578
Negative [C]	0.201816	0.148916	0.273506
Positive [W]	29	12.243502	68.689497
Negative [W]	0.425	0.318367	0.567349

The entry 'NaN' in any of the above cells means that the calculation cannot be performed because the values entered include one or more instances of zero.

[Technical note](#) on calculation of confidence intervals.

Printable Report

ANEXO 7

Imágenes de soporte de la realización de las adecuaciones del Laboratorio de Infección e Inmunidad de la Facultad de Salud de la Universidad Surcolombiana. Nótese la instalación de la cabina de bioseguridad clase II B2 que se encuentra totalmente operativa. El informe de instalación del equipo respectivo se adjunta al final del actual anexo.



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FORTALECIMIENTO DE CAPACIDADES INSTALADAS DE CIENCIA Y
TECNOLOGÍA DE LA GOBERNACIÓN DEL HUILA Y LA UNIVERSIDAD
SURCOLOMBIANA PARA ATENDER PROBLEMÁTICAS ASOCIADAS
CON AGENTES BIOLÓGICOS DE ALTO RIESGO PARA LA SALUD
HUMANA EN EL DEPARTAMENTO DEL HUILA

[BPIN 2020000100145](#)

Carlos Fernando Narváez
Médico Inmunólogo
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Soporte gráfico
Octavo Informe Técnico Trimestral
Agosto de 2022
Neiva - Huila



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FACULTAD DE CIENCIAS DE LA SALUD

SOPORTES EN IMÁGENES DEL CUMPLIMIENTO DE LA ACTIVIDAD DENTRO DEL OBJETIVO ESPECÍFICO 2 (OE2): “ADELANTAR OBRAS DE ADECUACIÓN DE ESPACIOS”

Carlos Fernando Narvárez
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Facultad de Salud
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Neiva – Huila

Octavo Informe Técnico Trimestral
Agosto de 2022
Universidad Surcolombiana
Facultad de Salud – Programa de Medicina

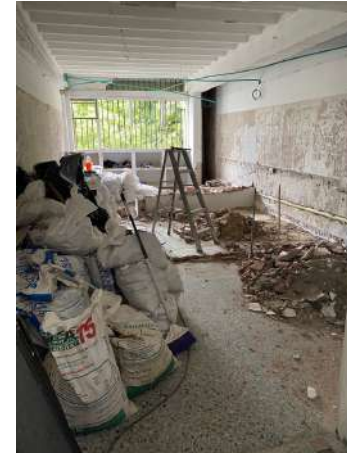
Imagen de instalaciones originales
(antes de las adecuaciones)



Reunión de inicio de obras
(Inicio de las adecuaciones)



Fase de demolición





Registro de asistencia a inicio de las obras de adecuación Laboratorio de Infección e Inmunidad - USCO

UNIVERSIDAD SURCOLOMBIANA GESTIÓN DE CALIDAD		REGISTRO Y CONTROL ASISTENCIA DE ACTIVIDAD Y/O EVENTO		Página 1 De 1			
CODIGO	EV-CAL-FO-03	VERSION	3	VIGENCIA	2019		
NOMBRE DE LA ACTIVIDAD Y/O EVENTO	Inicio de ejecución de adecuaciones		NOMBRE DEL EXPOSITOR	Laboratorio de Infección e Inmunidad	INTERNO	X	
OBJETIVO DE LA ACTIVIDAD Y/O EVENTO	Inicio de las obras de adecuaciones del Lab de Infección e Inmunidad						
LUGAR	Facultad de Salud - USCO		FECHA	10-Mayo/2022	HORA	9:30am	
"En mi calidad de titular de los datos personales anteriormente diligenciados, me permito manifestar mi autorización para su tratamiento por parte de la Universidad Surcolombiana, con la finalidad de ser utilizados en el contacto de otros eventos o servicios de la Universidad, incluyendo las finalidades del ámbito académico y administrativo propio de sus funciones. La Universidad Surcolombiana protege los datos aquí diligenciados, de acuerdo a lo previsto en la Ley 1581 de 2012, y a su Política de Protección de Datos Personales, la cual se debe consultar en la página www.usco.edu.co "							
N°	NOMBRES Y APELLIDOS	ENTIDAD/DEPENDENCIA/PROGRAMA ACADÉMICO	CORREO ELECTRÓNICO	TELEFONO No. EXT	TIPO DE ASISTENTE		FIRMA
1	Pedro Goveña	Planeación	Pedro.goveña@usco.edu.co			X	[Firma]
2	Angie Córdoba S.	Planeación	angie.cordoba@usco.edu.co			X	[Firma]
3	Alejandra Maná C.	Secre. Adm. Fac. Salud	ronia.mana@usco.edu.co			X	[Firma]
4	Yerson Esteban Tolo	Movul					[Firma]
5	Diego A. Noriega Rite						[Firma]
6	Alberto Valderrama	Mantenimiento				X	[Firma]
7	Andrés Felipe Bahamón	Movul	andresbahamon@gmail.com				[Firma]
8	Oberson, Douglas	Movul	oberson.pedraza@usco.edu.co				[Firma]
9	Alexander Luna Linares	Movul	Eng. Alexander@unil.edu.co				[Firma]
10	CARLE GALLARDO A.	MTD	Schulzgalardo@unil.edu.co			X	[Firma]
11	Claudia B. Vargas Cardón	Proff. Apoyo SST	Claudia.vargas@usco.edu.co			X	[Firma]
12	Roberto Coronado G	SSDH	rcoronado97@notmail.com	315 323 3121			[Firma]
13	Daniel Santiago Ramirez	Tec. Obras Civiles	v20191179331@usco.edu.co			X	[Firma]
14	Carlos F. Norwicz	Medicina-USCO	cfnorwicz@usco.edu.co	871 9310	X		[Firma]
15							

* Tipo de asistente: DP: Docente Planta, DO: Docente Ocasional, DC: Docente Cátedra, DI: Docente Visitante, AD: Administrativo, TO: Trabajador Oficial, ES: Estudiante, MR: Médico Residente, CO: Contratista, EX: Externo

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Imágenes del proceso de ejecución de las adecuaciones del Laboratorio de Infección e Inmunidad de la Universidad Surcolombiana, Facultad de Salud. Junio – Julio 2022.



El antes y después:

Antes de las adecuaciones



Después de las adecuaciones





Otras imágenes



Cabina de bioseguridad
clase II B2 instalada

Evento de entrega de las adecuaciones del Laboratorio de Infección e Inmunidad - USCO

A.



B.



C.



D.



E.



F.



Placa de entrega de las adecuaciones



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Enlaces con soporte audio-visual

<https://www.facebook.com/100069064454983/posts/pfbid02k1tidmdFdV2KXQYu6BF79KuTY6f2iojZNNvRoXGgoyYd3RaH7BUD7aP8kzTizsNHI/?d=n>

<https://fb.watch/eCmAGI7FH5/>

<https://www.facebook.com/USCOoficial/videos/5359288874154496/>

<https://diariodelhuila.com/inversion-en-ciencia-y-tecnologia-asciende-a-113-000-millones-de-pesos/>

ANEXO 8

Actividades de difusión del impacto regional del proyecto en los medios de comunicación.

Diario del Huila

Hoy es 23 de Agosto del 2022



Diario del Huila



Inversión en Ciencia y Tecnología asciende a \$113.000 millones de pesos

Jul 30, 2022

Diario del Huila [Inicio](#) > [Regional](#) > Inversión en Ciencia y Tecnología
asciende a \$113.000 millones de pesos

DIARIO DEL HUILA, REGIONAL

Proyectos como el fortalecimiento de las capacidades instaladas en los laboratorios de Salud Pública del Departamento y de la Universidad Surcolombiana, se benefician de esta inversión realizada por el Gobierno Departamental.

Se cumplió este viernes la ceremonia de entrega de los nuevos espacios adecuados de la división de inmunología en la Facultad de Salud de la Universidad Surcolombiana, como parte de los proyectos financiados con fondos del Gobierno Departamental a través del Sistema General de Regalías.

El recorrido por las instalaciones y acto protocolario fueron presididos por el Viceministro de Talento y Apropiación Social de Conocimiento del Ministerio de Ciencia, Tecnología e Innovación, Nelson Andrés Calderón, quien exaltó la articulación y liderazgo regional para lograr materializar importantes proyectos que beneficiarán ampliamente a la población huilense.

“Hoy estamos dejando en el Huila las capacidades instaladas que beneficiarán a la sociedad. El departamento, la Universidad Surcolombiana, los investigadores de la región han fomentado el fortalecimiento de laboratorios de pruebas diagnósticas para el sistema de salud, que además del Covid podrá identificar otras enfermedades tropicales” afirmó el viceministro.

Dijo además que el Huila ha contado con asignación de recursos por el orden de 113 mil millones de pesos para el desarrollo de proyectos de ciencia, tecnología e innovación, “como este laboratorio que es de nivel II, que seguirá en proceso de fortalecimiento, es una muestra de las inversiones que benefician directamente a la sociedad”.

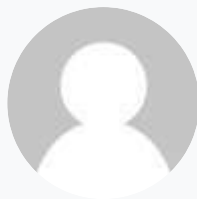
Capacidad instalada en laboratorios para diagnósticos en salud

Carlos Fernando Narváez, Jefe de la División de Inmunología de la Universidad Surcolombiana señaló que este proyecto surgió de la necesidad de resolver la capacidad técnica y tecnológica para identificar el genoma viral de SarsCov2.

“Contamos ahora con equipos de alta tecnología y de las mejores marcas empleadas en la identificación de virus, en el cultivo de virus, que nos permiten saber si una persona está infectada o tiene alguna enfermedad. Además del Covid19, podremos reconocer otras enfermedades virales como el Dengue que tanto afecta el departamento” sostuvo Carlos Fernando Narváez.

Así mismo, destacó que, “En solo un año del bienio se logró la aprobación de importantes recursos para ciencia y tecnología. Con la entrega de éste proyecto, los laboratorios para análisis de pruebas de Covid19 colocaron al Huila como uno de los primeros en tomar y analizar muestras en el territorio, fuimos pioneros al servicio del Sur colombiano” manifestó Sergio Andrés Trujillo, Coordinador del Sistema General de Regalías del Departamento.

El Huila ha desempeñado un papel muy importante en la gestión de proyectos que han surgido de las necesidades sentidas de los sectores académicos, de salud y productivos, inversiones que se verán reflejadas en el progreso de la región.



Autor: WebMasterDH



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JOHAN ROJAS | 23 AGO, 2022

Una apuesta histórica: el 'gana gana' de la región central

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Diario del Huila con lo último en información

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DH ADS



The advertisement features a blue and white diamond-patterned background. At the top left, there is a graphic of the Earth with the text "DH Radio" in a stylized font. Below this, the main text reads "Las noticias, los personajes y la opinión crítica de los hechos." At the bottom left, there are icons for YouTube, Facebook, and Instagram. On the right side, there is a photograph of a woman with long dark hair wearing a yellow top, standing in front of a roller coaster track.



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REGIONAL

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12 NOV, 2021

En el Huila falleció un menor por Covid-19

El departamento ya completa nueve casos de mortalidad en menores por causa del Sarscov2. Con un llamado urgente a...

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Diario del Huila

Editora del Huila SA - Diario del Huila

Fundado el 8 de Agosto de 1966

Fundadores:

Max Duque Gómez - Max Duque Palma

Directora

María Pía Duque Rengifo

Gerente General

Luisa María Duque Cerón

gerente@diariodelhuila.com

Calle 8 No. 6-30 Neiva-Colombia

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**Gobernación del Huila**

29 de julio a las 10:58 ·



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Luis Enrique Dussán

29 de julio a las 10:55

¡Es Histórico! inversión de \$113.000 millones de pesos en Ciencia y Tecnología por parte del gobierno "Huila Crece"

Se destacan proyectos como el fortalecimiento de las capacidades instaladas en los laboratorios de Salud Pública del Departamento y de la Universidad Surcolombiana.

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Enviar mensaje



página



Parche Saludable



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Desde La U



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SENA Caquetá

Interés

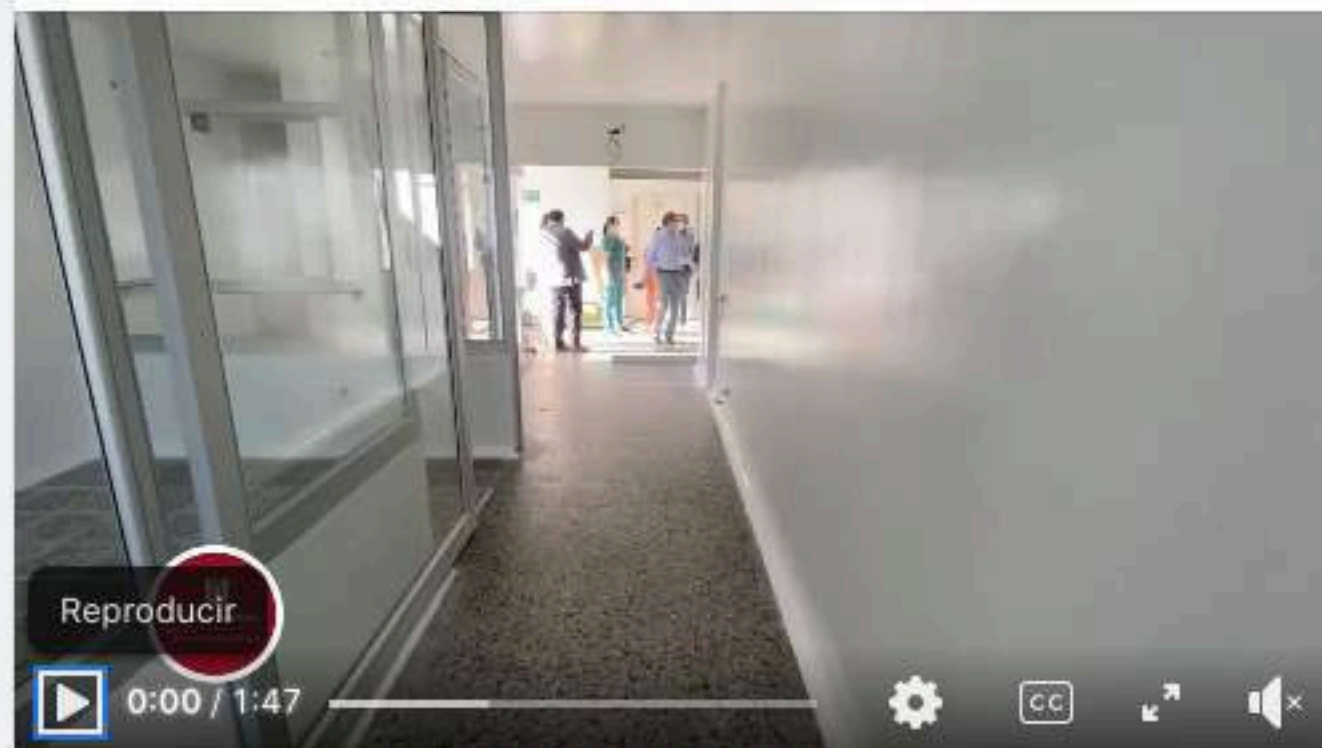


Facultad de Salud -USCO

30 de julio a las 12:15 · 🌐

#BuenasNoticiasEnNuestraFacultad

Con la participación del Viceministro de Talento y Apropiación Social de Conocimientos del Ministerio de Ciencia, Tecnología e Innovación, se llevó a cabo la ceremonia de entrega de los nuevos espacios adecuados en la División de Inmunología de la Facultad de Ciencias de la Salud, esto como producto del proyecto financiado por la Gobernación del Departamento del Huila a través del Sistema General de Regalías.

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Universidad Surcolombiana

2 de agosto a las 18:52 ·

Recibimos la visita de Nelson Andrés Calderón Guzmán, Viceministro de Talento y Apropiación Social (e) de Minciencias, para recibir el Laboratorio de Inmunología, así como conocer los avances e impacto del proyecto "Fortalecimiento de Capacidades Instaladas de Ciencia y Tecnología de la Gobernación del Huila y la Universidad Surcolombiana, para atender problemáticas asociadas con agentes biológicos de alto riesgo, para la salud humana en el departamento.

[#NoticiaUSCO](#)[#U... Ver más](#)

12

3 veces compartido

ANEXO 9

Este Anexo corresponde a una grabación de la reunión de cierre de la visita de pares académicos nacionales e internaciones en miras a obtener la reacreditación institucional de alta calidad de la Universidad Surcolombiana. Se destaca en ella el enorme impacto regional que ha tenido la ejecución de la propuesta. Esto tuvo un positivo efecto en el informe de la visita.

ANEXO 10

Actividades de Control Social, difusión y socialización de resultados del proyecto. Soporte gráfico de la presentación del fortalecimiento del Laboratorio de Infección e Inmunidad a la comunidad y a instituciones educativas de la ciudad. Adicionalmente se presenta soporte gráfico de las actividades de transferencia técnica y de habilidades en la realización de ensayos moleculares y serológicos para virus emergentes entre personal de las entidades aliadas.



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[BPIN 2020000100145](#)

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Soporte gráfico
Octavo Informe Técnico Trimestral
Agosto de 2022
Neiva - Huila



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SOPORTES EN IMÁGENES DE LAS ACTIVIDADES DE CONTROL SOCIAL, DIFUSIÓN DE RESULTADOS Y TRANSFERENCIA DE CONOCIMIENTO

Carlos Fernando Narváez
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Séptimo Informe Técnico Trimestral
Universidad Surcolombiana
Facultad de Salud – Programa de Medicina

Actividad de control social



Presentación del proyecto y sus logros

A.



B.



C.



D.



E.



Presentación de resultados ante pares académicos durante la visita para acreditación internacional del programa de Medicina (sup A-B) y Reacreditación de Alta calidad Institucional de la Universidad Surcolombiana (inf C-D).

Presentación del proyecto y sus logros a la comunidad. Informe Gráfico de Visita Alumnos Colegio Colombo – Sueco de Neiva





Registro de asistencia visita de socialización

UNIVERSIDAD SURCOLOMBIANA GESTIÓN DE CALIDAD		REGISTRO Y CONTROL ASISTENCIA DE ACTIVIDAD Y/O EVENTO		Página 1 De 1													
CODIGO	EV-GAL-FO-03	VERSIÓN	3	VIGENCIA	2019												
NOMBRE DE LA ACTIVIDAD Y/O EVENTO	Visita de adecuaciones Lab infección inmu			NOMBRE DEL EXPOSITOR	Carlos F. Narváez												
OBJETIVO DE LA ACTIVIDAD Y/O EVENTO	Presentar los adecuaciones del Lab de infección e Inmunidad																
LUGAR	Laboratorio de Infección e Inmunidad	FECHA	03 agosto	HORA	8:30 am												
<p>"En mi calidad de titular de los datos personales anteriormente diligenciados, me permito manifestar mi autorización para su tratamiento por parte de la Universidad Surcolombiana, con la finalidad de ser utilizados en el contacto de otros eventos o servicios de la Universidad, incluyendo las finalidades del ámbito académico y administrativo propio de sus funciones. La Universidad Surcolombiana protege los datos aquí diligenciados, de acuerdo a lo previsto en la Ley 1581 de 2012, y a su Política de Protección de Datos Personales, la cual se debe consultar en la página www.usco.edu.co".</p>																	
N°	NOMBRES Y APELLIDOS	ENTIDAD/DEPENDENCIA/ PROGRAMA ACADÉMICO	CORREO ELECTRÓNICO	TELÉFONO No. EXT	* TIPO DE ASISTENTE										FIRMA		
					DP	DO	DC	DI	AD	TO	ES	MR	CO	EX			
1	Santiago Fajardo Rojas		sfajardo640@gmail.com													X	
2	Julieith Perdomo		perdomi701ieth@gmail													X	
3	Anagie Ossa Rojas		ankorossa@gmail.com													X	
4	Laura Guzmán Rodríguez		lauragutmanrj2@gmail.com													X	
5	Laura Sofía Cherry		laura.sofia.cherry@unama.edu.co													X	
6	Isabel Sofía Leguizamón		gmepralieu21@gmail													X	
7	Gabriel Herrera F															X	
8	Pablo Yerani Betancourt S.		pbacnabolar@gmail.com													X	
9	William Perdomo Diaz		wilamfermando.perdomo@gmail.com													X	
10	Ean Sebastian Rivera H.		iseba.sruech@gmail.com													X	
11	Alison Fernanda Puentes A.		Aliferpuentes@gmail.com													X	
12	Ana María Cherry Loreno		anamariacherryf13@gmail.com													X	
13	Juan David Lizcano		Pirco Perdomo@gmail.com													X	
14	Juan Esteban Díaz A		Juan333.Esteban.dia@gmail.com													X	
15																X	

* Tipo de asistente: DP: Docente Planta, DO: Docente Ocasional, DC: Docente Cátedra, DI: Docente Visitante, AD: Administrativo, TO: Trabajador Oficial, ES: Estudiante, MR: Médico Residente, CO: Contratista, EX: Externo

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[Handwritten signature]

Actividades de transferencia técnica del Inmunoensayo para IgM e IgG DENV basado en NS1



Transferencia y práctica del ELISA para IgM e IgG DENV basado en NS1 desde el Laboratorio de Infección e Inmunidad al personal de la Secretaría de Salud del Huila.



Listado de asistencia transferencia de conocimiento y habilidades ensayos moleculares y serológicos para *Flavivirus*

UNIVERSIDAD SURCOLOMBIANA GESTIÓN DE LA CALIDAD		REGISTRO Y CONTROL ASISTENCIA DE ACTIVIDAD Y/O EVENTO		Página 1 De 1			
CODIGO	EV-CAL-FO-03	VERSIÓN	4	VIGENCIA	2022		
NOMBRE DE LA ACTIVIDAD Y/O EVENTO	Capacitación en la Metodología de ELISA "In House" para la detección de IgM e IgG NS1 para DENV			NOMBRE DEL EXPOSITOR	Carlos Fernando Narváez		
OBJETIVO DE LA ACTIVIDAD Y/O EVENTO	Familiarizarse con la técnica de ELISA "In House" para la detección de IgM e IgG NS1 para DENV y así posteriormente aplicarlo según necesidad.						
LUGAR	Laboratorio de Infección e Inmunidad	FECHA	27 de julio de 2022	HORA	08:00:00		
<p>"En mi calidad de titular de los datos personales diligenciados, me permito manifestar mi autorización para su tratamiento por parte de la Universidad Surcolombiana, con la finalidad de ser utilizados en el contacto de otros eventos o servicios de la Universidad, incluyendo las finalidades del ámbito académico y administrativo propio de sus funciones. La Universidad Surcolombiana protege los datos aquí diligenciados, de acuerdo a lo previsto en la Ley 1581 de 2012, y a su Política de Protección de Datos Personales, la cual se debe consultar en la página www.usco.edu.co".</p>							
N°	NOMBRES Y APELLIDOS	DOCUMENTO DE IDENTIDAD	ENTIDAD/DEPENDENCIA/PROGRAMA ACADÉMICO	CORREO ELECTRÓNICO	TELÉFONO No. EXT	* TIPO DE ASISTENTE	FIRMA
1	Pilda García / A	55234422	LSP	wilda.garcia.15@gmail.com	31884244	X	[Firma]
2	Zachary (García) / ano	53071811	LSP	zachary.garcia@univ.edu@gmail.com	32154244	X	[Firma]
3	Richard M. Peña	51858443	I&I Lab	Richard.marcela.pena@usco.edu.co	32153344	X	[Firma]
4	Sandra L. Delgado U.	41961768	I&I Lab	Sandra.delgado@usco.edu.co	30003544	X	[Firma]
5	Carmen Yilena Carón	36290788	IPI Lab	Carmen-Carón@USCO.edu.co	31442430	X	[Firma]
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

* Tipo de asistente: DP: Docente Planta, DO: Docente Ocasional, DC: Docente Cátedra, DV: Docente Visitante, AD: Administrativo, TO: Trabajador Oficial, ES: Estudiante, MR: Médico Residente, CO: Contratista, EX: Externo

Vigilado Mineducación

La versión vigente y controlada de este documento, solo podrá ser consultada a través del sitio web institucional www.usco.edu.co, link Sistema Gestión de Calidad. La copia o impresión diferente a la publicada, será considerada como documento no controlado y su uso indebido no es de responsabilidad de la Universidad Surcolombiana.

ANEXO 11

Soportes de la vinculación del Laboratorio de Infección e Inmunidad a la Red Nacional de Diagnóstico COVID-19 desde diciembre de 2020, avalado por el INS.



UNIVERSIDAD

SURCOLOMBIANA

FACULTAD DE CIENCIAS DE LA SALUD

**SOPORTES EN IMÁGENES DE LA VINCULACIÓN DEL
LABORATORIO DE INFECCIÓN E INMUNIDAD A LA
RED DE REGISTRO DE LABORATORIOS (RELAB) Y A
LA RED NACIONAL DE DIAGNÓSTICO COVID-19**

Carlos Fernando Narvárez
Médico Inmunólogo
Jefe División de Inmunología
Facultad de Salud
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Neiva – Huila

Octavo Informe Técnico Trimestral
Agosto de 2022
Universidad Surcolombiana
Facultad de Salud – Programa de Medicina

Soportes de la vinculación del Laboratorio de Infección e Inmunidad a la Red Nacional de Diagnóstico COVID-19

Estos son los laboratorios autorizados para realizar pruebas de COVID-19 en Colombia

El INS tiene un listado de 188 laboratorios autorizados para el procesamiento de pruebas COVID.



Pruebas PCR en Bogotá. Foto: Altabla de Bogotá

Por: Juan David Ríos | 29 de Julio, 2021

Debido a la cantidad de pruebas PCR de coronavirus que se han reportado como falsificadas porque fueron modificadas para ingresar a diferentes países, el Instituto Nacional de Salud (INS) reiteró el **listado de 188 laboratorios autorizados** para realizar este tipo de test, además de antígenos, para la detección del COVID-19.

PUBLICIDAD

Lo más reciente

Economía Hace 13 minutos

INS Instituto Nacional de Salud

Inicio | Transparencia y acceso a la información pública | Atención y Servicios a la ciudadanía | Participa | ¿Qué hacemos? | Normativa | Centro de comunicaciones

COVID-19 en Colombia

Corte 21-07-2022 5:00 p.m.

Información para la vigilancia | Información para laboratorios

Panorama | Genome | Casos | Departamento | Municipio | Poblaciones | Muestras | Comunicaciones | Notas

Reporte diario | Conglomerados | Laboratorios

¿Cómo está conformada la Red de Laboratorios para PCR en Colombia?

Biblioteca sobre pruebas (PCR, rÁpidas, antígenos y CLIA-ELISA)

Accede a BioMuestras

Los laboratorios de verificación de desempeño de validación secundaria deben confirmar la utilidad y el funcionamiento de una prueba, en los escenarios propuestos que son: diagnóstico. Para el control de calidad en Bogotá y la verificación de desempeño en municipios de la zona de influencia de Bogotá, desde el 1 de agosto del 2021, se va a evidenciar en un nivel más amplio la realización de pruebas de diagnóstico de COVID-19. Conocer la calidad y pertinencia de las pruebas de diagnóstico de COVID-19 es fundamental para garantizar la calidad de los resultados de las pruebas de diagnóstico de COVID-19.

Estos son los laboratorios aut: x Noticias coronavirus-laboratori x +

ins.gov.co/Noticias/Paginas/coronavirus-laboratorios.aspx


Capacidad máxima declarada
96,000

Laboratorios adjuntos para diagnóstico de COVID-19
227


Procesamiento por tipo laboratorio

LSP - Colaboradores SP 25.77%
Instituto Nacional de Salud 3.80%
Red de Laboratorios EAPB 70.43%

% de procesamiento



Laboratorios de procesamiento PCR por departamento



Huila
5 Laboratorios
LDSP Huila
Laboratorio Hospital Hermandad Moncaleano
Laboratorio Clínico Angeles Biología Molecular IPS
Laboratorio Infección e Inmunidad Univ Surcolombiana
Laboratorio Aidalab S.A.S

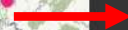
Search

Departamento o distrito	Laboratorio	Tipo	Correo
HUILA	LDSP Huila	LDSP	clermeoa_crarry@yahoo.es
HUILA	Laboratorio Clínico Angeles Biología Molecular IPS	Laboratorio Privado	magdalenafala@hotmail.com
HUILA	Laboratorio Hospital Hermandad Moncaleano	Laboratorio Privado	leonmercedes.otero@ruhimp.gov.co
HUILA	Laboratorio Infección e Inmunidad Univ Surcolombiana	SP	charvaez@usco.edu.co
LA	Laboratorio Aidalab S.A.S	Laboratorio Privado	calidad@aidalab.com
MADEIRA	Laboratorio Olimpus	Laboratorio Privado	calidad@olimpuslab.com
MACDALENA	Universidad del Magdalena	SP	lydianquecasto@hotmail.com

Descargue aquí el listado

Si un laboratorio de la red ampliada de diagnóstico de COVID-19 o que quiera hacer parte de ella, desea implementar RT-PCR o cualquier metodología de detección molecular, este debe realizar un ejercicio de verificación técnica que demuestre el cumplimiento de los criterios de desempeño definidos por el fabricante. De esta manera, el INS avala su uso en el laboratorio que realizó la verificación bajo sus condiciones técnicas y estándares de calidad, y no se debe entender como una autorización para su uso inmediato en otros laboratorios. Cada laboratorio debe demostrar su propia competencia para usar la técnica que otro laboratorio de la red ampliada ya verificó, teniendo siempre como premisa el aseguramiento de la calidad de los resultados.

Ver punta flecha roja



<https://www.ins.gov.co/Noticias/Paginas/coronavirus-laboratorios.aspx>

Listado de laboratorios avalados: proveído por el INS



Departamento o distrito	Laboratorio	Tipo	Correo	Dirección física
AMAZONAS	LDSP Amazonas	LDSP	isp@amazonas.gov.co	Calle 10 No. 6-63 Leticia - Amazonas
ANTIOQUIA	Universidad Nacional sede Medellín Laboratorio One Health	SP	coord_cw@unai.unal.edu.co	Calle 75 # 79A - 51 Bloque M15 Facultad de Minas. Ingeominas Universidad Nacional de Colombia, Medellín
ANTIOQUIA	LDSP Antioquia	LDSP	sandraines.cano@antioquia.gov.co	Carrera 72A #. 78B-141 Piso 3 y 4. Barrio Robledo Medellín - Antioquia
ANTIOQUIA	SURA	Laboratorio Privado	contactoayudas@sura.com.co	Calle 27 #45-109 Ayudas Diagnósticas SURA piso 4. Medellín
ANTIOQUIA	Universidad Antioquia	SP	djmicrobiologia@uda.edu.co dilaboratorio@uda.edu.co	Calle 67 # 53 -108 bloque 5 of 418
ANTIOQUIA	Corporación para Investigaciones Biológicas	SP	directorgeneral@cib.org.co azuluaga@cib.org.co	Carrera 72 A # 78 B - 141. Medellín
ANTIOQUIA	Hospital Pablo Tobón	Laboratorio Privado	sjaramillo@hptu.org.co	Hospital Pablo Tobón Uribe Calle 78 b 69 - 240 Laboratorio clínico torre B piso 3 Medellín
ANTIOQUIA	Clinica SOMER Rionegro	Laboratorio Privado	fabiorpo@clinicasoner.com corozco@clinicasoner.com	Clinica Somer Calle 38 N 54A-35 Rionegro Antioquia
CORDOBA	Laboratorio Clínico Especializado Humalib SAS	Laboratorio Privado	gerencia@humalib.com	Calle 22 #2-15 Montería - Córdoba
CORDOBA	Laboratorio Universidad Sinu sede Córdoba	Laboratorio Privado	catalinatovar@unisinu.edu.co	Carrera 1w #38-153 bloque 5 Laboratorio de investigaciones Biomédicas Barrio Juan XXIII Montería - Córdoba
CUNDINAMARCA	Agrosavia CI Tibaitatá	Laboratorio Privado	ramartinez@agrosavia.co	Km 14 Vía Mosquera, Cundinamarca
CUNDINAMARCA	Hospital universitario de la samaritana	LDSP	laboratorio.lider@hus.org.co	cra 8 # 0- 29 Bogotá
CUNDINAMARCA	Hospital Cardiovascular de Cundinamarca	SP	Laboratorio@hccsa.com.co	Cra 1 este No. 31-58 8. San Mateo Soacha
CUNDINAMARCA	LDSP Cundinamarca	Laboratorio Privado	nathaly.sierra@cundinamarca.gov.co	Calle 21 A No. 70-10 Parque Industrial Montevideo Bogotá D.C.
CUNDINAMARCA	Laboratorio Hospital Nuestra Señora de las Mercedes - Funza	Laboratorio Privado	coordinadorlabhnsnm@outlook.com	Calle 11 No. 9 - 99 Funza- Cundinamarca
GUAJIRA	Hospital San Jose de Maicao	Laboratorio Privado	lab.biologiamolecularg@esssanjosedemaicao.gov.co	Calle 16 # 39A bis -31 Salida a Rioacha frente al Batallón
GUAJIRA	Laboratorio IPS Sol Wayuu	Laboratorio Privado	gerencia@ipsisolvayuu.com.co	Calle 13 No 11-64 Local 1 Riohacha , Guajira
GUAJIRA	LDSP Guajira	LDSP	ispguajira@gmil.com	Calle 12 # 8-19 Riohacha - Guajira
HUILA	LSPD Huila	LDSP	clemencia_charry@yahoo.es	Carrera 20 No. 58-36 Barrio Calixto Leyva Neiva Huila
HUILA	Laboratorio Clínico Angeles Biología Molecular IPS	Laboratorio Privado	magdalena.falla@hotmail.com	Calle 7#88-10 Neiva Huila
HUILA	Laboratorio Hospital Hernando Moyano	Laboratorio Privado	leonormercedesotero@uhmp.edu.co	Calle 9 N. 15-25 Neiva - Huila
HUILA	Laboratorio Infección e Inmunidad Univ Surcolombiana	SP	cfnarvaez@usc.edu.co	Calle 9#14-02 Facultad de Salud, Universidad Surcolombiana, Neiva, Huila.

LABORATORIOS QUE ESTÁN AVALADOS PARA REALIZAR DIAGNÓSTICO DE SARS-COV2

CORTE 13 ENERO DE 2021

TIPO	NOMBRE	Acta Inicio	Depto	No
SP	Instituto Nacional de Salud		Bogotá	1
LDSP	LSP Distrital	13/03/2020	Bogotá D.C.	2
SP	Universidad Rosario (Sede Quinta de Mutis)	28/03/2020	Bogotá D.C.	3
LDSP	LSP Valle del Cauca	28/03/2020	Valle del Cauca	4
LDSP	LDSP Antioquia	29/03/2020	Antioquia	5
LDSP	LDSP Atlántico	30/03/2020	Atlántico	6
LDSP	LDSP Cesar	05/04/2020	Cesar	7
Venta Servicios	SURA	08/04/2020	Antioquia	8
SP	Universidad de Cartagena Laboratorio UNIMOL	08/04/2020	Bolívar	9
LDSP	LSP Nariño	08/04/2020	Nariño	10
SP	Universidad Industrial de Santander	08/04/2020	Santander	11
Venta Servicios	Laboratorio Higuera Escalante	08/04/2020	Santander	12
SP	Universidad Simón Bolívar	11/04/2020	Atlántico	13
SP	Universidad del Cauca	11/04/2020	Cauca	14
SP	Agrosavia CI Tibaitatá	11/04/2020	Cundinamarca	15
SP	Universidad Tecnológica de Pereira	11/04/2020	Risaralda	16
SP	Universidad de Sucre	11/04/2020	Sucre	17
SP	Instituto Colombiano Medicina Tropical ICMT Sede Sabaneta	18/04/2020	Antioquia	18
SP	Universidad Nacional sede Medellín Laboratorio One Health	18/04/2020	Antioquia	19
SP	Universidad de Antioquia	18/04/2020	Antioquia	20
Venta Servicios	Hospital Pablo Tobón	18/04/2020	Antioquia	21
Venta Servicios	Laboratorio Echavarría	18/04/2020	Antioquia	22
Venta Servicios	Compensar calle 26	18/04/2020	Bogotá D.C.	23
Venta Servicios	Compensar calle 63	18/04/2020	Bogotá D.C.	24
SP	Universidad de los Andes Laboratorio Gencore	18/04/2020	Bogotá D.C.	25
Venta Servicios	Fundación Santa fé	18/04/2020	Bogotá D.C.	26
SP	Universidad del Bosque	18/04/2020	Bogotá D.C.	27
Venta Servicios	Laboratorio Molecular de Clínica Colsanitas Keralty	18/04/2020	Bogotá D.C.	28
Venta Servicios	SURA	18/04/2020	Bogotá D.C.	29
Venta Servicios	Laboratorios COLCAN	18/04/2020	Bogotá D.C.	30
Venta Servicios	Fundación Valle de Lili	18/04/2020	Valle del Cauca	31
Venta Servicios	Hospital Universitario del Valle "Evaristo Garcia"	18/04/2020	Valle del Cauca	32
Venta Servicios	Imbanaco	18/04/2020	Valle del Cauca	33
Venta Servicios	Universidad del Valle	18/04/2020	Valle del Cauca	34
Venta Servicios	Laboratorio Las Américas	22/04/2020	Antioquia	35
Venta Servicios	IDIME	22/04/2020	Bogotá D.C.	36
Venta Servicios	Clínica SOMER Rionegro	23/04/2020	Antioquia	37
SP	Laboratorio Dirección Sanidad Policía Nacional	23/04/2020	Bogotá D.C.	38
SP	Universidad de Caldas	23/04/2020	Caldas	39
Venta Servicios	Hospital Fundación San Vicente de Paul	24/04/2020	Antioquia	40
Venta Servicios	Laboratorio SYNLAB Colombia	24/04/2020	Antioquia	41
Venta Servicios	Laboratorio Clínico e Inmunológico Lorena Vejarano	24/04/2020	Bogotá D.C.	42
Venta Servicios	Hemato Oncólogo	24/04/2020	Valle del Cauca	43
SP	Universidad de Córdoba	27/04/2020	Córdoba	44
SP	Corporación para Investigaciones Biológicas	29/04/2020	Antioquia	45
Venta Servicios	Hospital Universitario San Ignacio	29/04/2020	Bogotá D.C.	46
SP	Laboratorio Dirección Sanidad Ejército	29/04/2020	Bogotá D.C.	47
Venta Servicios	Laboratorio Clínico Citisalud	02/05/2020	Atlántico	48
SP	Universidad del Atlántico Laboratorio LIMB	02/05/2020	Atlántico	49
Venta Servicios	Analizar Laboratorio Clínico Automatizado S.A.S	02/05/2020	Bogotá D.C.	50
SP	Laboratorio Clínico ECOPELROL	02/05/2020	Santander	51
Venta Servicios	Analicemos laboratorio Clínico Especializado	02/05/2020	Tolima	52
Venta Servicios	Asoclinic - Cauceseco	02/05/2020	Valle del Cauca	53
LDSP	LDSP Arauca	07/05/2020	Arauca	54
Venta Servicios	Laboratorio Continental	11/05/2020	Atlántico	55
SP	Universidad del Magdalena	11/05/2020	Magdalena	56

Venta Servicios	Laboratorio Nancy Flórez	15/05/2020	Cesar	57
LDSP	LDSP Huila	18/05/2020	Huila	58
SP	Agrosavia CI La Libertad	23/05/2020	Meta	59
LDSP	LSP Tolima	23/05/2020	Tolima	60
Venta Servicios	Fundación Cardiovascular De Colombia Zona Franca	26/05/2020	Santander	61
Venta Servicios	Lab Christus Sinergia Salud -Clin Farallones	26/05/2020	Valle del Cauca	62
SP	Universidad Cooperativa de Colombia Sede Medellín	28/05/2020	Antioquia	63
Venta Servicios	Universidad de Antioquia Laboratorio LIME	30/05/2020	Antioquia	64
Venta Servicios	Hospital San Pedro	31/05/2020	Nariño	65
Venta Servicios	Clínica Clinizad	01/06/2020	Nariño	66
Venta Servicios	Universidad Sinú sede Cartagena	04/06/2020	Bolívar	67
SP	Universidad Nacional - Laboratorio Micobacterias	06/06/2020	Bogotá D.C.	68
SP	Universidad Nacional - Laboratorio Max Planck	06/06/2020	Bogotá D.C.	69
Venta Servicios	Laboratorio ADILAB	08/06/2020	Antioquia	70
Venta Servicios	Laboratorio IMAT Instituto médico de alta tecnología S.A.S	08/06/2020	Córdoba	71
SP	Universidad Nacional - Laboratorio Biotecnología IBUN	11/06/2020	Bogotá D.C.	72
Venta Servicios	Instituto Nacional de Cancerología	11/06/2020	Bogotá D.C.	73
Venta Servicios	Laboratorio Cristiam Gram	11/06/2020	Cesar	74
Venta Servicios	Unidad Hematológica Especializada	11/06/2020	Norte de Santander	75
Venta Servicios	Hospital Universitario Clínica San Rafael	12/06/2020	Bogotá D.C.	76
Venta Servicios	Laboratorio Clínica Médicos SA	17/06/2020	Cesar	77
Venta Servicios	Laboratorio Médico de Referencia SAS	19/06/2020	Antioquia	78
Venta Servicios	Hospital Maria Inmaculada	19/06/2020	Caquetá	79
Venta Servicios	Hospital Departamental de Villavicencio	19/06/2020	Meta	80
Venta Servicios	Lab Servicio de Diagnóstico Médico SDM	19/06/2020	Valle del Cauca	81
Venta Servicios	Clínica de Occidente	20/06/2020	Valle del Cauca	82
Venta Servicios	Lab Comfandi	24/06/2020	Valle del Cauca	83
Venta Servicios	Laboratorio UNIGEM	29/06/2020	Antioquia	84
Venta Servicios	Biotecgen Laboratorio Clínico	29/06/2020	Bogotá D.C.	85
Venta Servicios	Fundación Cardio Infantil	29/06/2020	Bogotá D.C.	86
SP	Universidad de Pamplona	29/06/2020	Norte de Santander	87
SP	laboratorio del Instituto Distrital de Ciencia, Biotecnología e Innovación en Salud IDCIBIS	03/07/2020	Bogotá D.C.	88
Venta Servicios	Laboratorio Investigación Hormonal	03/07/2020	Bogotá D.C.	89
LDSP	LDSP Boyacá	04/07/2020	Boyacá	90
SP	Instituto Colombiano Medicina Tropical ICMT sede Apartado	08/07/2020	Antioquia	91
Venta Servicios	Laboratorio Sinergia Global	10/07/2020	Bogotá D.C.	92
Venta Servicios	Hospital Santa Clara	10/07/2020	Bogotá D.C.	93
SP	Laboratorio ICA	11/07/2020	Santander	94
SP	Laboratorio Universidad de Santander UDES Laboratorio LIBB	13/07/2020	Santander	95
Venta Servicios	Hospital Regional de la Orinoquia - HORO	16/07/2020	Casanare	96
SP	Universidad Lasallista	17/07/2020	Antioquia	97
Venta Servicios	Laboratorio Bonnadona	17/07/2020	Atlántico	98
Venta Servicios	Fundación Grupo de Estudio Barranquilla - Laboratorios Reyfals	19/07/2020	Atlántico	99
SP	Universidad de la Salle	20/07/2020	Bogotá D.C.	100
Venta Servicios	Laboratorio de Gencell Pharma SAS	22/07/2020	Bogotá D.C.	101
Venta Servicios	Laboratorio de la Clínica Los Nogales	22/07/2020	Bogotá D.C.	102
Venta Servicios	Laboratorio Clínico del Hospital Infantil Los Ángeles	22/07/2020	Nariño	103
Venta Servicios	Laboratorio Yamina Cumplido	23/07/2020	Sucre	104
Venta Servicios	Bienestar IPS	25/07/2020	Atlántico	105
Venta Servicios	Laboratorio Yunis Turbay	25/07/2020	Bogotá D.C.	106
Venta Servicios	Laboratorio Clínica del Norte	29/07/2020	Atlántico	107
Venta Servicios	Laboratorio Echavarría sede Bogotá	29/07/2020	Bogotá D.C.	108
Venta Servicios	Laboratorio Hospital Hernando Moncaleano	01/08/2020	Huila	109
Venta Servicios	Laboratorio Clínica Medihelp	03/08/2020	Bolívar	110
Venta Servicios	Laboratorio Clínica de la Costa	06/08/2020	Atlántico	111
Venta Servicios	Laboratorio Respirar	06/08/2020	Chocó	112
Venta Servicios	Hospital Erasmo Meoz	10/08/2020	Norte de Santander	113

Venta Servicios	Laboratorio Clínica de Putumayo	10/08/2020	Putumayo	114
LDSP	LSP Norte de Santander	12/08/2020	Norte de Santander	115
Venta Servicios	Laboratorio Asoclinic sede Buenaventura	13/08/2020	Valle del Cauca	116
Venta Servicios	Laboratorio Hospital San Rafael Tunja	14/08/2020	Boyacá	117
Venta Servicios	Laboratorio Carvajal IPS	18/08/2020	Boyacá	118
Venta Servicios	Hospital San Jose de Maicao	18/08/2020	Guajira	119
Venta Servicios	Laboratorio Clínico Subred Integrada Servicios de Salud Norte E.S.E Hospital Simon Bolivar	24/08/2020	Bogotá D.C.	120
Venta Servicios	Laboratorio Los Cobos	25/08/2020	Bogotá D.C.	121
Venta Servicios	Laboratorio Clínica Shaio	29/08/2020	Bogotá D.C.	122
Venta Servicios	Clínica Infantil Colsubsidio	29/08/2020	Bogotá D.C.	123
Venta Servicios	Procardio Hospital Cardiovascular	29/08/2020	Cundinamarca	124
Venta Servicios	Hospital Civil Ipiales	29/08/2020	Nariño	125
Venta Servicios	Laboratorio PECET - Universidad de Antioquia	01/09/2020	Antioquia	126
Venta Servicios	Laboratorio Angel (Synlab)	02/09/2020	Valle del Cauca	127
Venta Servicios	Lab Clínica Nueva (Idime)	02/09/2020	Valle del Cauca	128
LDSP	LDSP Córdoba	03/09/2020	Córdoba	129
Venta Servicios	Laboratorio CIDEIM	03/09/2020	Valle del Cauca	130
Venta Servicios	Laboratorio Alife Health	05/09/2020	Bogotá D.C.	131
Venta Servicios	Laboratorio Clínico Kheneyzir Fayad SAS	11/09/2020	Atlántico	132
LDSP	LDSP Amazonas	9/13/2020	Amazonas	133
Venta Servicios	Clinaltec	18/09/2020	Tolima	134
Venta Servicios	Lab Clínica Rafael Uribe Uribe(Idime)	13/09/2020	Valle del Cauca	135
Venta Servicios	Lab Colcan sede Cali	18/09/2020	Valle del Cauca	136
Venta Servicios	Laboratorio Clínica Sanitas - Sebastian de Belalcazar	18/09/2020	Valle del Cauca	137
Venta Servicios	Laboratorio Clínica Iberoamericana (Sanitas)	19/09/2020	Atlántico	138
Venta Servicios	Laboratorio del Valle	25/09/2020	Nariño	139
Venta Servicios	Laboratorio Clínico de Servicios Médicos Olimpus IPS	26/09/2020	Magdalena	140
Venta Servicios	Laboratorio Hospital Deptal Nariño	26/09/2020	Nariño	141
Venta Servicios	Laboratorio Hospital Universitario Samaritana	03/10/2020	Cundinamarca	142
SP	Laboratorio del Instituto de Genética Humana de la facultad de Medicina de la Universidad Pontificia Javeriana	06/10/2020	Bogotá D.C.	143
Venta Servicios	Laboratorio clínico de la Fundación Clínica Infantil Club Noel	08/10/2020	Valle del Cauca	144
Venta Servicios	Laboratorio Clínica Universitaria Medicina Integral SAS - ALVEN	21/10/2020	Córdoba	145
Venta Servicios	Laboratorio CAFAM	22/10/2020	Bogotá D.C.	146
Venta Servicios	Laboratorio Saludpass SA	28/10/2020	Bogotá D.C.	147
Venta Servicios	Laboratorio Central Referencia Clin Colsanitas	30/10/2020	Bogotá D.C.	148
Venta Servicios	Laboratorio Clínico Angeles Biología Molecular IPS	06/11/2020	Huila	149
LDSP	Laboratorio de Salud Pública Departamental Quindio	12/11/2020	Quindio	150
Venta Servicios	Laboratorio Clínico Hematológico Ltda	18/11/2020	Antioquia	151
Venta Servicios	Laboratorio Biotest	02/12/2020	Atlántico	152
Venta Servicios	Laboratorio Clínica Universitaria Pontificia Bolivariana	03/12/2020	Antioquia	153
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La salud es de todos

Minsalud

ANEXO 12

Soportes de la vinculación del Laboratorio de Infección e Inmunidad de la Universidad Surcolombiana a la plataforma de Registro de Laboratorios a nivel nacional (RELAB). Se muestra registro de pruebas validadas ofrecidas. De notar, se demuestra el incremento en las capacidades para el abordaje molecular y serológico de enfermedades emergentes a nivel regional, en particular las producidas por infección con Flavivirus y SARS-CoV-2.



	ID	Departamento	Municipio	Entidad	Área	Prueba	Matriz	Metodologia	MetodoEnsayo	Documento normativo	Objetivo prueba	Fecha verificación	Fecha registro	Oferta activa	Estado
Modificar Cambiar_oferta Detalles Anular	70029	HUILA	NEIVA	UNIVERSIDAD SURCOLOMBIANA	VIROLOGIA	DENGUE ANTICUERPOS IgM	PLASMA	ELISA			Investigación		2022-08-22 09:11	Si	Activo
Modificar Cambiar_oferta Detalles Anular	70028	HUILA	NEIVA	UNIVERSIDAD SURCOLOMBIANA	VIROLOGIA	DENGUE ANTICUERPOS IgG	PLASMA	ELISA			Investigación		2022-08-22 09:10	Si	Activo
Modificar Cambiar_oferta Detalles Anular	66344	HUILA	NEIVA	UNIVERSIDAD SURCOLOMBIANA	VIROLOGIA	SARS-CoV-2 (COVID-19) ANTICUERPOS IgM	PLASMA	ELISA			Investigación		2022-05-24 15:19	Si	Activo
Modificar Cambiar_oferta Detalles Anular	66343	HUILA	NEIVA	UNIVERSIDAD SURCOLOMBIANA	VIROLOGIA	SARS-CoV-2 (COVID-19) ANTICUERPO IgG (S1 Y S2)	PLASMA	ELISA			Investigación		2022-05-24 15:18	Si	Activo
Modificar Cambiar_oferta Detalles Anular	65088	HUILA	NEIVA	UNIVERSIDAD SURCOLOMBIANA	VIROLOGIA	SARS-CoV-2 (COVID-19) DETECCION DE ACIDOS NUCLEICOS	HISOPADO NASOFARINGEO	RT PCR			Diagnóstica		2022-05-07 09:14	Si	Activo

ANEXO 13

Artículo científico publicado en la revista Viral Immunology. En él se analiza el efecto de Dengue virus sobre plaquetas humanas y sus precursores para tratar de entender la trombocitopenia que caracteriza la infección por DENV.



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Dengue Virus and Platelets: From the Biology to the Clinic

Paula X. Losada,¹ Isabel DeLaura,² and Carlos F. Narváez¹

Abstract

Dengue is one of the most important vector-borne viral illnesses found in tropical and subtropical regions. Colombia has one of the highest rates of dengue cases in the Americas. Severe dengue virus (DENV) infection presents with capillary leakage, hemorrhage, and organ compromise, eventually leading to death. Over the years, there have been many efforts to develop a vaccine that guarantees protective immunity, but they have been partially successful, as such immunity would need to guarantee protection against four distinct viral serotypes. Absolute platelet count is a laboratory parameter used to monitor the clinical progression of DENV, as infection is often accompanied by thrombocytopenia. Although this finding is well described with respect to the natural history of the disease, there are various hypotheses as to the cause of this rapid decrease, and several *in vivo* and *ex vivo* models have been used to explain the effect of DENV infection on platelets and their precursors. DENV infects and activates platelets, facilitating their elimination through recognition by phagocytic cells and peripheral margination. However, infection also affects the precursors in the bone marrow by modulating megakaryopoiesis. The objective of this article is to explore various proposed mechanisms of DENV-induced thrombocytopenia to better understand the pathophysiology and clinical presentations of this highly relevant viral infection.

Keywords: Dengue virus (DENV), platelets, megakaryocytes, cytokine, MEG-01

Introduction

DENGUE VIRUS (DENV) INFECTION is associated with high morbidity and mortality among both children and adults in tropical and subtropical regions. DENV is a public health issue, as it is transmitted by *Aedes* mosquitoes (primarily *Aedes aegypti*) and therefore can impact a high percentage of the population, imposing a large burden on health care systems (39). During 2019, the incidence of dengue in the Americas was >321 dengue cases per 100,000 people. A total of 1,538 deaths were also reported and the highest recorded number of infections in the history of dengue in the region (119).

Early clinical management is fundamental for avoiding progression to the severe form of the disease. However, there is currently no specific antiviral treatment available. Vaccination has been proposed as an effective preventative strategy. In 1944 and 1945, Kimura and Hotta (45) and

Sabin and Schlesinger (97) developed the first monovalent vaccines. At present, the only DENV vaccine approved in some countries for use in humans is Dengvaxia[®], a chimeric tetravalent vaccine with a live virus (CYD-TDV) that uses yellow fever viral strain 17D as a base, with recombinant genes—premembrane (*PrM*) and envelope (*E*)—along with each of the four DENV serotypes (42). This vaccine has been controversial owing to differences in its efficacy against different viral serotypes and an increase in the risk of severe illness when given to young children previously unexposed to DENV (43,109).

There are other vaccines in the final phases of clinical trials. One of these is the Takeda vaccine candidate (TAK-003), a vaccine that consists of a DENV-2 virus base with chimeric DENV-DENV (53,117). Other vaccines include a live attenuated (LAV Delta 30), DENV180 protein subunit (DEN1-80E), and DENV DNA vaccine, also in advanced stages of study (32,33).

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In recent decades, there have been continued efforts to understand and treat DENV infection. Although it is accepted that prevention and management of the infection are key, it is also fundamental to understand the impact of DENV at the cellular and tissue levels. Accordingly, observational and experimental studies have explored this topic (3,34,48,70,84). The current classification of DENV infection uses not only clinical signs and symptoms but also certain laboratory parameters such as hepatic enzymes. Laboratory tests may be used for diagnostics or to follow the disease course (116). For example, a decrease in absolute circulating platelet count has been correlated with severe forms of the disease in animal models and humans (71,82).

A fast and significant decrease in the absolute count number of circulating platelets is a common pathophysiological phenomenon with clinical consequences during DENV infection (56,116). Thus, it has been proposed that this specific cell type is a preferential direct and indirect target of viral infection (80,100). Several mechanisms, including the effects of DENV infection on bone marrow platelet precursors or peripheral vascular consumption of mature platelets, have been proposed to explain the decrease in the absolute number of this cell type in circulation during DENV infection (6,88). The objective of this article is to discuss the current state of knowledge about DENV-platelet interactions and the possible causes of thrombocytopenia during DENV infection.

Can DENV Infect Human Platelets, and How Does This Affect Its Pathogenesis?

The first attempts at the viral infection of platelets were conducted in the 1950s and consisted of exposing human platelets to influenza virus inducing their agglutination (26,73) and then, enabling the capture of the first images of viral infection of platelets using electronic microscopy (30).

Human platelets are small cytoplasmic fragments ranging 2–4 μm in diameter derived from bone marrow megakaryocytes. They travel through blood vessels and contribute to primary hemostasis and subsequent coagulation through activation and aggregation. Mitochondria, endoplasmic reticulum, lysosomes, and between 50 and 80 granules are found in the cytoplasm of each platelet (36). The granules can be grouped into three major types: α -granules, dense granules, also called δ -granules, and lysosome-like granules. The α -granules contain proteins such as chemokines, cytokines, and growth factors necessary for platelet function. They contain small molecules such as adenosine diphosphate (ADP), serotonin, polyphosphates, glutamate, histamine, and calcium, which are necessary for hemostasis. The third type of granule functions similar to lysosomes, which vary in molecular cargo, biogenesis, trafficking, and exocytosis. Other organelles present in platelets include peroxisomes and T granules, characterized by the upregulation of Toll-like receptor 9 (TLR9) during pro-platelet production (36,110). Furthermore, platelet lysosomes contain glycohydrolases along with enzymes that degrade glycoproteins. Although the principal role of platelets is to maintain hemostasis, they also play an important role in other pathophysiological processes, such as tumor growth, metastasis, inflammatory response, and host defenses, as they are an important source of cytokines (19,60).

The presence of DENV in platelets and its capacity to enter these cells have been studied for years. It has been confirmed that platelets can bind and internalize infectious agents (19,20,41). However, the impact of DENV on these cells is only partially known. The recognition of viral pathogen-associated molecular patterns (PAMPs) through pattern recognition receptors (PRRs) facilitates the production of interferon (IFN)-I, whose stimulating antiviral and immune properties are beneficial for viral elimination. In the short term, IFNs impact hematopoiesis, resulting in temporary aplasia and potential alteration of megakaryopoiesis. This decrease in the regulation of hematopoiesis is likely a protective mechanism of the microenvironment that limits damage to the marrow compartment or progenitor cells during the process of elimination of infected cells (74,83).

In vitro models have been used to identify platelet mechanisms of viral binding and internalization through proteoglycans such as heparan sulfate and DC-SIGN, a C-type lectin receptor. It has been shown in human platelet precursors *in vitro* that once the virus has entered the cells, it begins with a replicative cycle and the translation of viral proteins, thus continuing to replicate its genome, and finally assembling new virions (8).

Once infected, platelets increase the expression of cell membrane proteins such as CD40 ligand (CD40L), CD42b, CD62P, and major histocompatibility complex class I (MHC-I). Evaluation of these interactions using primary human platelets and DENV serotype 2 (DENV-2) has shown a significant increase in CD40L in the culture supernatant and greater secretion of cytokines such as granulocyte-macrophage colony-stimulating factor, interleukin (IL)-6, IL-8, IL-10, and tumor necrosis factor (TNF- α) compared with controls (77).

One method of confirming viral replication, apart from genome amplification (positive or negative single-strand RNA) using real-time RT-PCR (RT-qPCR), is through the detection of structural and nonstructural proteins. Among these, nonstructural protein 1 (NS1) has emerged as a useful alternative. This protein is not present in the infecting viral particle, but it is expressed and actively secreted by infected cells. Although it is known to be essential for viral replication, the exact mechanisms through which it participates in this process are not entirely known (24). NS1 is also a protein highly utilized in current diagnostic evaluation.

Furthermore, it is possible to isolate platelets in peripheral blood for subsequent *in vitro* infection with DENV. Methods such as RT-qPCR can then be used to quantify viral RNA and western blots can be used to identify the NS1 protein, confirming replication and translation of the viral genome in thrombocytes (100). However, it has also been observed that infectious viral particles do not accumulate in platelets or their precursors in culture (50). Previous findings suggested that although platelets support DENV replication, they do not assemble or release even very low titers of infecting viral particles (50,100).

It is not clear whether platelets contribute to the transport and dissemination of DENV infection *in vivo* or if, on the contrary, they aid in host defense against the infection. For now, the debate continues, and the hypothesis has been proposed that the DENV-platelet interaction may have a dual role depending on the infecting serotype and the environment in which platelets and megakaryocytes are found (35).

Platelet activation has also been reported in human natural DENV infection, as demonstrated by the increase in expression of membrane proteins such as platelet integrin receptor (α Ib β 3), lysosomal marker CD63, and granular marker CD62P (P-selectin) (71).

Platelets are involved in the pathophysiology of DENV infection through partially described mechanisms. First, as immune cells, platelets enable the host immune system to activate α -granules, which release cytokines such as platelet factor 4 (PF4), RANTES, platelet-derived growth factor, and transforming growth factor-beta (TGF- β) (65). Second, thrombocytes can impact the integrity of endothelial cells that coat blood vessel walls, because platelets and their precursors secrete vascular endothelial growth factor A (VEGF-A), which alters the phenotype of endothelial cells, thus increasing vascular permeability. This activation explains in part the capillary leakage classically observed in patients with severe forms of DENV infection. Significantly increased circulating levels of VEGF-A have been found in patients with more severe forms of the illness (38,64,107).

The rapid and transient thrombocytopenia and subsequent recovery observed in DENV infection suggest that short-lived immune factors such as cytokines are responsible, at least partially, for this process (102). DENV infection induces a significant systemic cytokine response secreted from innate and adaptive compartments, and the rapid and transient increase in cytokines has been proposed as a mechanism related to endothelium activation, vascular leakage, and severe clinical forms of DENV infection (14,18,103). Some of these cytokines, such as IL-8, IL-10, TNF- α , and soluble receptor-II (sTNFR_{II}) (40,58), have been negatively correlated with the platelet count.

The application of recombinant human IL-10 to healthy adults resulted in thrombocytopenia. This effect was associated with a decrease in the number of megakaryocytes in bone marrow rather than a decrease in platelet half-life owing to peripheral sequestration (101). In addition, the application of TNF- α induces endothelial damage with platelet aggregation mediated by von Willebrand factor (vWF) and adhesion molecules in a human melanoma model (92). Caspase activation (Caspase 3, particularly) has been observed in murine platelets exposed *in vivo* or *in vitro* to TNF- α , a finding that supports cell death as a mechanism involved in TNF- α -mediated thrombocytopenia (85). Thus, TNF- α is one of the cytokines clearly associated with thrombocytopenia through a decrease in platelet half-life in the periphery.

Nevertheless, many questions remain unanswered regarding thrombocytopenia induced by DENV infection, such as the *in vivo* contribution of the spleen and endothelium or the mechanisms of thrombocytopenia during primary or secondary infection (57). Purified primary platelet models have been used for decades and have been useful for elucidating direct viral effects on these cells. However, they have important limitations, such as platelet activation induced by the purification process.

New models for the study of thrombocytopenia in DENV are needed (12). The development of both immunodeficient and immunocompetent murine models will be key. As has been evaluated in models of autoimmune thrombocytopenia, adoptive transfer from infected individuals could provide additional information on humoral and cellular factors responsible for the drop-in platelet numbers during DENV

infection. In addition, the analysis of platelet functionality through evaluation of its aggregation capacity is another important source of information on the role of platelets in DENV infection (111).

Effects of DENV Infection on Platelet Precursors

Another effect of DENV infection is bone marrow suppression. The reduction of megakaryopoiesis and granulopoiesis in the first 4 days of infection accounts for the decrease in leukocyte and platelet counts in peripheral blood (13). Once the critical phase of the illness has passed, recovery of the absolute cell count occurs notably in conjunction with clinical improvement, as hyperplasia of megakaryocytes, myeloid cells, and erythrocytes has been observed after the 6th day following symptom onset (76,114). Understanding the causal mechanisms of the bone marrow changes and their impact on thrombopoiesis is key to understanding DENV pathology, offering an opportunity to impact both diagnosis and management and, therefore, the patient's outcome.

Hematopoietic stem cells and megakaryocytes represent ~0.4% of the total cellular contents of bone marrow; as a result, these cells are difficult to isolate and study. The use of cell lines derived from these types of precursors, which partially resemble the conditions observed *in vivo*, has been considered an alternative to evaluating the interaction between DENV and human platelet precursors *in vitro*.

During the initial stages of platelet progenitor maturation, glycoproteins GPIIb (CD41a) and GPIIIa/ β 3 (CD61) are early markers of megakaryocytes (MK) differentiation (63). At this time, they are the most abundant proteins on the platelet precursor surface and they form a functional dimeric complex that recognizes and binds to fibrinogen and vWF (94). During the course of maturation, they start to express a second vWF receptor, which consists of three chains called GPIb α , GPV, and GPIX, known in conjunction as CD42b, a marker that is commonly used to differentiate between immature and mature MKs (63,99).

Megakaryocyte and erythrocyte precursors have been described taking a role in the immunity during DENV infection (17). There is evidence of changes in the morphology and proportions of the cell populations in bone marrow infected with DENV (75). The first reports by Bierman and Nelson showed that patients with severe dengue had few to no MKs during hospitalization per analysis of their bone marrow aspirate. Then, during the convalescent phase, both their immature and mature MK counts had recovered (13), which gave rise to further studies that have confirmed that DENV infection is accompanied by a decrease in central thrombopoiesis in human and animal models (76,87). These observations are most consistent with early suppression of megakaryocytopoiesis in the bone marrow (76).

The primary precursor cells necessary to explore these theories must be obtained using bone marrow aspiration—a painful and invasive procedure. Thus, many studies have used components of peripheral blood, which are more practical and easier to obtain. One study reported a positive correlation between viral load in the plasma of patients with acute dengue and the circulation of CD61-positive cells (an MK marker), as well as with an increase in IFN- γ levels in serum (46).

MK and megakaryocytic cell lines respond to viral infections and recognize viral PAMPs, thus secreting high

levels of IFN- α and β (4), which reduce the production of platelets *in vitro* through autocrine IFNAR signaling. Apart from the reduction in platelet production, it is expected that the direct infection of MK, the involvement of PRR, and locally induced cytokine signaling change the phenotype of platelet progeny generated during the infection; this would influence immune and inflammatory processes mediated by platelets in the periphery (51).

In vivo studies, starting with modeling infection through viral inoculation of humanized mice and using quantification of viral RNA and flow cytometry to detect intracellular expression of E viral protein in bone marrow samples, have shown that 1.5% of immature human megakaryocytes and 35% of mature megakaryocytes become infected with DENV during infection (112). Furthermore, the pattern of selective expression of membrane proteins is necessary for DENV to infect this cellular population, thus affecting the dynamics of thrombopoiesis.

Models of MK and platelet infection have been proposed *ex vivo*. Hematopoietic precursor cells from the umbilical cord stimulated with a cocktail of cytokines consisting of thrombopoietin, IL-9, IL-6, and SCF, differentiate into immature MKs. After treatment with DENV, these cells maintained a constant level of viral RNA that persisted, but did not increase, over time (112).

In vitro studies have advanced our understanding of the impact of infection on host cells. The use of cell lines provides an opportunity to analyze the impact of viral infection: MEG-01 cells have been particularly useful, as they are megakaryoblastic cells obtained from the bone marrow of a patient with chronic myelogenous leukemia in blast crisis (78). DENV-2 propagates efficiently and produces viral particles when infecting this cell line (28). Infection has been detected through the presence of viral RNA inside MEG-01 cells, confirming that these cells are susceptible to DENV-2 virus infection (8). This cell line differentiates into mature platelets under certain conditions, making it an attractive *in vitro* model to study the effect of DENV infection on thrombopoiesis.

One characteristic of platelet progenitors that appears to be influenced by the infection is the endomitosis, where mitosis is interrupted in the middle of anaphase and the cell enters a new mitotic cycle. As a consequence, the number of chromosomes increases inside a single-lobed nucleus, resulting in polyploidy. This condition allows for the amplification of the cellular genome to support the synthesis of the proteins necessary for cellular growth and the formation of platelets. Thus, DENV infection disturbs platelet formation and may contribute to the genesis of thrombocytopenia (5). The production of platelet-like particles derived from MEG-01 cells has been demonstrated through treatment with phorbol 12-myristate 13-acetate (PMA), a potent activator of protein kinase C (PKC) (106).

Owing to the multiple actions of PKC isoforms, the mechanisms of PMA-induced differentiation of MEG-01 cells are very diverse. In general, it is used to recreate particles similar to mature platelets *in vitro* from the MEG-01 cell line. These particular cells show an increase in β 1-tubulin, which is important for the late phase of MK differentiation and the early phase of circulating platelet production. Therefore, PMA-treated MEG-01 cells are considered a valid model to study the process of platelet production (47).

The maturation stage of platelet development in the context of DENV infection appears to influence the cellular capacity of viral replication. Existing theories propose that differentiation of platelet progenitors results in increased replication of DENV, as a greater number of viral RNA copies are observed in MEG-01 cells that have been infected and then differentiated with PMA than in those that do not undergo differentiation. Nonstimulated MEG-01 cells are susceptible to DENV infection, whereas MEG-01 cells that are differentiated and prestimulated with PMA are refractory to infection and viral replication (8). In conclusion, DENV infects primary and cell line-derivate platelet progenitors and affects the process of megakaryopoiesis, which directly, or in combination with other factors, results in the decrease in platelet counts as observed in patients with dengue.

What Explains Thrombocytopenia in DENV Infection?

An understanding of the complex interactions between the virus, platelets, and other cellular populations is necessary to understand the context of DENV infection. Platelets and leukocytes are fundamental for primary hemostasis and coagulation. The leukocyte-platelet interaction is modulated by various proteins, such as CD42 (glycoprotein GPIb) on platelets, macrophage-1 antigen (MAC1, also known as α M β 2), complement receptor 3 (CR3), CD11b, and integrin α -M (ITGM). Once interactions are established, phagocytic cells are recruited to the inflamed endothelium, where they identify damaged or altered thrombocytes and eliminate them (11).

It has been shown that isolated platelets from the peripheral blood of patients in the acute phase of DENV infection are activated and trapped by monocytes, demonstrating a role of monocytes and macrophages in DENV thrombocytopenia (34,98). However, when inactivated by prostaglandin E2 (PGE2), phagocytosis is halted (37), as PGE2 inhibits platelet activation and aggregation, thus inhibiting various stages in the activation of the arachidonic acid metabolic cascade. This cascade normally activates adenylyl cyclase, increasing the levels of AMPc, a crucial mediator of platelet aggregation (29). In turn, both this signaling pathway and the consequent cellular interactions are impacted by DENV infection of platelets.

The host immune response results in decreased peripheral platelet counts in DENV-infected patients through several partially understood pathways. Three complementary and not mutually excluding theories have been proposed (Fig. 1): A. A decrease in platelet production as a consequence of selective suppression in bone marrow (Fig. 1A). B. An increase in peripheral platelet consumption (Fig. 1B). C. Platelet lysis occurring through the formation of immune complexes (9) (Fig. 1C).

DENV can directly infect and induce cell death of platelet precursors in bone marrow (10) (Fig. 1A). In addition, the application of domain III fragment from the E protein induces suppression of mice and human platelet precursors *in vivo* and *in vitro*, respectively (59), demonstrating that viral replication or whole dengue viral particles are not a necessary requirement for bone marrow suppression (Fig. 1A). Immune factors released in response to viral infection such as IFNs can induce significant effects to the megakaryopoiesis.

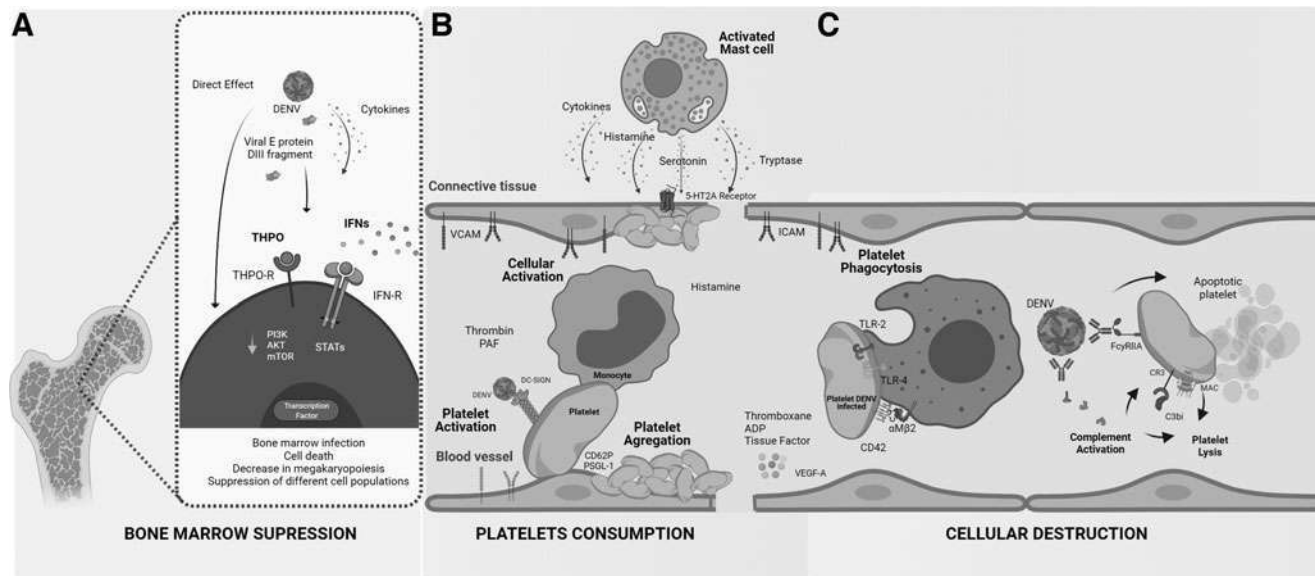


FIG. 1. Cellular and molecular interactions contributing to thrombocytopenia during DENV infection. **(A)** In the short term, whole DENV or viral fragments such as domain III (DIII) of E protein can induce apoptosis of platelet precursors in the bone marrow. Also, cytokines (such as IFNs) signaling can affect the megakaryocytic lineage during infection. In the context of viral infection, IFN dimerization of receptor subunits causes the activation of proteins such as Tyk2 and Jak1, which eventually activate signal transducers, and transcription activators such as the STAT family of proteins. This mediates the activation of transcriptional proteins that play important functional roles in the development and differentiation of these cells, fibrinogen binding, P-selectin externalization, and cell aggregation. Other pathways involved in the THPO signaling such as the PI3K/AKT/mTOR axis have been recently shown to be inhibited by DENV infection. **(B)** Circulating platelets can be activated by monocytes, by the pathogen through receptors that mediate viral entrance, and by factors such as thrombin, which then releases molecules such as PAF as well as coagulation cascade activators such as thromboxane, ADP, and tissue factor. This induces platelet aggregation via the interaction between molecules such as P-selectin (CD62P) and PSGL-1 found in endothelial cells. Products released from activated mast cells such as serotonin, cytokines, and histamine induce subsequent activation of vascular endothelial cells, which increases platelet aggregation. Mast cells also release tryptase, an enzyme with the capacity to disrupt intercellular endothelial junctions. **(C)** Infected platelet–phagocytic cell interactions are conducive to platelet phagocytosis through recognition by molecules such as Toll-like receptors, and this interaction can enhance the inflammatory response. Cellular lysis can be mediated through antibodies that can activate the classical complement pathway owing to the formation of the MAC, the presence of CR3, or the recognition of antigen-specific antibodies against the virus by Fc γ RIIA. ADP, adenosine diphosphate; CR3, complement receptor 3; DENV, dengue virus; MAC, membrane attack complex; PAF, platelet-activating factor; PSGL-1, P-selectin glycoprotein ligand-1; THPO, thrombopoietin. The Figure was created with BioRender.

Various studies in human and murine models have demonstrated that alterations in the signaling pathway of IFNs contribute to the depletion of hematopoietic progenitors, thus affecting the signaling pathways of canonical and noncanonical transcription factors, which may act as a myeloid differentiation checkpoint in hematopoietic stem and progenitor cells (68) (Fig. 1A). In support of this, rapid and remarkable thrombocytopenia depending on the type I IFN expressed in bone marrow is induced after injection of TLR agonists *in vivo* (93).

It has also been proposed that a decrease in IFN- γ levels results in depletion of stem cells and therefore suppresses marrow function (68,72). A simultaneous decrease in granulocytopenia and megakaryopoiesis is a strong indicator of marrow dysfunction at the level of hematopoietic pluripotent stem release cells or that the virus may simultaneously affect progenitors of two or more cell lineages. Recently, other new signaling pathways highly related to megakaryopoiesis such as the PI3K/AKT/mTOR axis have been shown to be modulated by DENV infection (55) (Fig. 1A).

In support of the theory of peripheral platelet consumption (Fig. 1B), patients with DENV infection may develop disseminated intravascular coagulation (DIC), a condition caused by the continual activation of the coagulation cascade and fibrinolytic system. In DIC, circulating platelets are activated by multiple factors, such as thrombin, which then release a variety of immune-stimulating molecules, such as histamine and platelet-activating factor, as well as coagulation cascade activators, such as thromboxane, ADP, and tissue factor (Fig. 1B). The consumption of procoagulant factors contributes to one of the frequent complications of infection—hemorrhagic syndrome—which is one definition of a severe presentation of the illness (31,116).

The other mechanism proposed to explain thrombocytopenia during DENV infection involves antibody-mediated peripheral destruction of platelets (Fig. 1C). A unique feature of DENV is that it has four different serotypes. Although these serotypes are structurally related, the generated protector host response is homotypic; that is, infection with one serotype does not generate long-lasting protection against the other three (44).

However, during secondary DENV infection, preexisting antibodies—particularly those against viral proteins prM and E—facilitate efficient binding of immature and mature viral particles to cells that express Fc receptors (95). Platelets express the Fc γ RIIA receptor (Fig. 1C). The binding of anti-prM-DENV complexes makes platelets susceptible to immune destruction. Platelet-immunoglobulin M or platelet-immunoglobulin G interactions are also important to explain DENV-mediated thrombocytopenia and the more severe presentations of this disease, such as those occurring during secondary DENV infection (79).

On the contrary, platelet-DENV complexes can bind to C3, IgM, and IgG, which subsequently facilitate their elimination through immune pathways (6,80,113) (Fig. 1C). It is important to take into account that the functions of C3 fragments and IgG include cellular opsonization and clearing (89). Flow cytometry has been used to evaluate proteins bound to the platelet membrane in supernatant from patients with acute dengue infection, showing an increase in binding of these proteins to the platelet membrane, which coincides with the timing at which the platelet count is the lowest, as recorded in the peripheral blood during days 4 and 6 of the disease course (80).

As the time course of the infection continues, platelets are activated and consequently decrease in count owing to recognition by phagocytic cells (Fig. 1C). Viral proteins on the membranes of infected platelets are recognized through interaction with Toll-like receptors 2 and 4 (TLR2, TLR4), which facilitate activation, aggregation, and adherence to endothelial cells and phagocytosis through macrophages (7,22) (Fig. 1C).

DENV can also activate platelets through lectin type C receptors, such as SLK 2, which at the same time stimulate macrophages and neutrophils through the CLEC 5A and TLR2 pathways (104,105). Neutrophils are then activated, forming neutrophil extracellular traps (NETs), which favor prothrombotic cells such as platelets, red blood cells, and molecules involved in intrinsic and extrinsic coagulation (89,104). NETs also activate platelets through TLR4, which generates a positive feedback circuit of additional NET and platelet activation.

Other proinflammatory and coagulation cascade-related molecules that interact with platelets are induced during dengue infection. After DENV infection, several cell lines and human primary cells show increased expression of the high mobility group box1 protein (HMGB1) (25,49,81), a nuclear damage-associated molecular pattern (DAMPs) released during necrosis and cell damage (118). Platelets are one of the main sources of HMGB1, and HMGB1 is also a strong inducer of platelet activation (96). Platelet activation through TLR by HMGB1 induces their aggregation by increasing peripheral sequestration. In addition, platelet-derived microvesicles containing HMGB1 have been shown to be a strong inducer of NETs (69), further increasing peripheral platelet loss.

A regulatory mechanism of the proinflammatory effects of HMGB1 is its uptake by thrombomodulin, an antithrombotic glycoprotein with anti-inflammatory effects that is expressed in endothelial cells and monocyte-macrophages (1). Although both circulating HMGB1 and thrombomodulin are increased in naturally infected patients with DENV and have been associated with the clinical severity of infection (2,16), their role in thrombocytopenia in dengue is not clear.

The role of mast cells and their secreted products has suggested a new and interesting mechanism of DENV-

induced thrombocytopenia (Fig. 1B). After *in vitro* treatment with DENV immunocomplex, human cord blood-derived mast cells and mast cell lines release cytokines such as TNF- α that induce expression of adhesion molecules such as vascular cell adhesion molecule-1 on the surface of endothelial cells (15) (Fig. 1B). Using mice deficient in mast cells and mast cells deficient in tryptophan hydroxylase-1 (an enzyme necessary for the production of serotonin in mast cells), strong platelet and endothelial activation mast cell dependent, with aggregation and a decrease in platelet number observed (66).

This effect is mediated through the 5HT_{2A} receptor (Fig. 1B), because drugs that selectively inhibit this receptor attenuated the thrombocytopenia (66,67). The increase of vascular permeability is a key clinical marker of severe dengue. Enzymes released after mast cells degranulation such as tryptase, have been associated with plasma leakage through disruption of endothelial tight junctions (91) (Fig. 1B). These findings indicate possibly new therapeutic targets.

Treatment of Thrombocytopenia During DENV Infection

At present, there is no specific antiviral treatment for infection with DENV, and treatment is focused on alleviating symptoms and treating clinical events during the infection, especially those that occur during the critical phase. Previous efforts have addressed the treatment of thrombocytopenia during DENV infection. It is now clear that there is no correlation between thrombocytopenia and the risk of bleeding during DENV infection (27,86), although there is a relationship of thrombocytopenia with the severity of the disease.

Therapeutic strategies have been developed for the prevention or treatment of bleeding related to thrombocytopenia during infection with DENV. To date, platelet transfusion has been the most studied. Prophylactic platelet transfusion in patients without bleeding has not shown significant reduction in the risk of developing subsequent bleeding. In addition, it is an expensive procedure with a high frequency of adverse events (23,62,115), such as urticaria, maculopapular rash, and pruritus (61). In addition, a high percentage of patients, usually those with lower platelet counts, do not respond or respond poorly to transfusion (52). Thus, there are clear indications for platelet transfusion in DENV infection based on a low platelet count with uncontrolled continuous bleeding and corrected coagulation factors, applying the same approach to patients with severe thrombocytopenia who must undergo a surgical procedure for other causes (108,116).

Other measures for the treatment of thrombocytopenia, such as intravenous immunoglobulin or thrombopoietin receptor agonists, have shown positive results, although strong evidence is still lacking in this regard (21,54,90). The above-mentioned limitations and lack of evidence support the need for controlled clinical trials for the treatment of bleeding associated with thrombocytopenia in patients with DENV infection.

The mechanisms summarized in this study contribute not only to understanding of thrombocytopenia but also to understanding the hemorrhage and capillary leakage, both critical clinical characteristics of DENV infection.

Conclusions

Platelets present in peripheral blood are a cellular subpopulation particularly impacted by DENV infection. DENV-platelet interactions are only partially understood, and many efforts over the last few years have made progress in understanding the pathophysiology and identifying the causal mechanisms of thrombocyte alterations. Three theories have been proposed to explain thrombocytopenia in DENV infection: selective bone marrow suppression, an increase in peripheral consumption, and immune complex-mediated elimination. Furthermore, DENV infection not only affects platelet counts but also activates these cells on a peripheral level and initiates several changes at a central level.

It is important to recognize that platelet infection impacts their functionality and can consequently induce alterations in hemostasis. It is also necessary to understand DENV infection as a multifactorial vascular illness, where a combination of immune system activation, coagulation, expression of anaphylatoxins and inflammatory proteins, and platelet sequestration and dysfunction results in a strong host response. Additional studies are necessary to explore the immunopathogenesis of DENV infection and to develop more options for diagnostics and treatment of a disease that, every year, takes the lives of thousands of people around the world, despite public health efforts to control the spread of the vector.

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References

1. Abeyama K, Stern DM, Ito Y, *et al.* The N-terminal domain of thrombomodulin sequesters high-mobility group-B1 protein, a novel antiinflammatory mechanism. *J Clin Invest* 2005;115:1267–1274.
2. Allonso D, Belgrano FS, Calzada N, Guzmán MG, Vázquez S, and Mohana-Borges R. Elevated serum levels of high mobility group box 1 (HMGB1) protein in dengue-infected patients are associated with disease symptoms and secondary infection. *J Clin Virol* 2012;55:214–219.
3. de Araújo JMG, Schatzmayr HG, de Filippis AMB, *et al.* A retrospective survey of dengue virus infection in fatal cases from an epidemic in Brazil. *J Virol Methods* 2009;155:34–38.
4. Arya RP, Lahon A, and Patel AK. Dengue virus induces interferon- β by activating RNA sensing pathways in megakaryocytes. *Immunol Lett* 2021;236:31–36.
5. Assinger A. Platelets and infection – an emerging role of platelets in viral Infection. *Front Immunol* 2014;5:649.
6. Azeredo EL De, Monteiro RQ, and Pinto LMD-O. Thrombocytopenia in dengue: interrelationship between virus and the imbalance between coagulation and fibrinolysis and inflammatory mediators. *Mediat Inflamm* 2015;2015:313842.
7. Balakrishna Pillai AK, Chu JJH, Mariappan V, and JeanPierre AR. Platelets in the pathogenesis of flavivirus disease. *Curr Opin Virol* 2022;52:220–228.
8. Banerjee A, Tripathi A, Duggal S, Banerjee A, and Vрати S. Dengue virus infection impedes megakaryopoiesis in MEG-01 cells where the virus envelope protein interacts with the transcription factor TAL-1. *Sci Rep* 2020;10:19587.
9. Barros TA da C, and de-Oliveira-Pinto LM. A view of platelets in dengue. In: *Thrombocytopenia*. London, UK: InTechOpen Limited, 2018.
10. Basu A, Jain P, Gangodkar S V, Shetty S, and Ghosh K. Dengue 2 virus inhibits in vitro megakaryocytic colony formation and induces apoptosis in thrombopoietin-inducible megakaryocytic differentiation from cord blood CD34+ cells. *FEMS Immunol Med Microbiol* 2008;53:46–51.
11. Begum F, Das S, Mukherjee D, Mal S, and Ray U. Insight into the tropism of dengue virus in humans. *Viruses* 2019;11:1136.
12. Bercovitz RS, Brenner MK, and Newman DK. A whole blood model of thrombocytopenia that controls platelet count and hematocrit. *Ann Hematol* 2016;95:1887–1894.
13. Bierman HR, and Nelson ER. Hematodepressive virus diseases of Thailand. *Ann Intern Med* 1965;62:867–884.
14. Braga EL, Moura P, Pinto LM, *et al.* Detection of circulating tumor necrosis factor-alpha, soluble tumor necrosis factor p75 and interferon-gamma in Brazilian patients with dengue fever and dengue hemorrhagic fever. *Mem Inst Oswaldo Cruz* 2001;96:229–232.
15. Brown MG, Hermann LL, Issekutz AC, *et al.* Dengue virus infection of mast cells triggers endothelial cell activation. *J Virol* 2011;85:1145–1150.
16. Butthep P, Chunchakan S, Tangnararatchakit K, Yoksan S, Pattanapanyasat K, and Chuansumrit A. Elevated soluble thrombomodulin in the febrile stage related to patients at risk for dengue shock syndrome. *Pediatr Infect Dis J* 2006;25:894–897.
17. Campbell RA, Schwertz H, Hottz ED, *et al.* Human megakaryocytes possess intrinsic antiviral immunity through regulated induction of IFITM3. *Blood* 2019;133:2013–2026.
18. Cardier JE, Mariño E, Romano E, *et al.* Proinflammatory factors present in sera from patients with acute dengue infection induce activation and apoptosis of human microvascular endothelial cells: possible role of TNF-alpha in endothelial cell damage in dengue. *Cytokine* 2005;30:359–365.
19. Chabert A, Hamzeh-Cognasse H, Pozzetto B, *et al.* Human platelets and their capacity of binding viruses: meaning and challenges? *BMC Immunol* 2015;16:26.
20. Chaipan C, Soilleux EJ, Simpson P, *et al.* DC-SIGN and CLEC-2 mediate human immunodeficiency virus type 1 capture by platelets. *J Virol* 2006;80:8951–8960.
21. Chakraborty S, Alam S, Sayem M, *et al.* Investigation of the efficacy and safety of eltrombopag to correct thrombocytopenia in moderate to severe dengue patients - a phase II randomized controlled clinical trial. *EClinicalMedicine* 2020;29–30:100624.

22. Chao CH, Wu WC, Lai YC, *et al.* Dengue virus non-structural protein 1 activates platelets via Toll-like receptor 4, leading to thrombocytopenia and hemorrhage. *PLoS Pathog* 2019;15:e1007625.
23. Chaudhary R, Khetan D, Sinha S, *et al.* Transfusion support to Dengue patients in a hospital based blood transfusion service in north India. *Transfus Apher Sci* 2006;35:239–244.
24. Chen HR, Lai YC, and Yeh TM. Dengue virus non-structural protein 1: a pathogenic factor, therapeutic target, and vaccine candidate. *J Biomed Sci* 2018;25:1–11.
25. Chen L-C, Yeh T-M, Wu H-N, Lin Y-Y, and Shyu H-W. Dengue virus infection induces passive release of high mobility group box 1 protein by epithelial cells. *J Infect* 2008;56:143–150.
26. Ching Lu W. Agglutination of human platelets by Influenza (PR8 strain) virus and Mumps virus. *Fed Proc* 1958; 17:446.
27. Chuansumrit A, Phimolthares V, Tardtong P, *et al.* Transfusion requirements in patients with dengue hemorrhagic fever. *Southeast Asian J Trop Med Public Health* 2000;31:10–14.
28. Clark KB, Hsiao H-M, Bassit L, *et al.* Characterization of dengue virus 2 growth in megakaryocyte–erythrocyte progenitor cells. *Virology* 2016;493:162–172.
29. Coulombe F, Jaworska J, Verway M, *et al.* Targeted prostaglandin E2 inhibition enhances antiviral immunity through induction of type I interferon and apoptosis in macrophages. *Immunity* 2014;40:554–568.
30. Danon D, Jerushalmy Z, and de Vries A. Incorporation of influenza virus in human blood platelets in vitro. Electron microscopical observation. *Virology* 1959;9: 719–722.
31. Davis RP, Miller-Dorey S, and Jenne CN. Platelets and coagulation in infection. *Clin Transl Immunol* 2016;5: e89.
32. Deng S-Q, Yang X, Wei Y, Chen J-T, Wang X-J, and Peng H-J. A review on dengue vaccine development. *Vaccines* 2020;8:63.
33. Durbin AP, Kirkpatrick BD, Pierce KK, Schmidt AC, and Whitehead SS. Development and clinical evaluation of multiple investigational monovalent DENV vaccines to identify components for inclusion in a live attenuated tetravalent DENV vaccine. *Vaccine* 2011;29:7242–7250.
34. Durbin AP, Vargas MJ, Wanionek K, *et al.* Phenotyping of peripheral blood mononuclear cells during acute dengue illness demonstrates infection and increased activation of monocytes in severe cases compared to classic dengue fever. *Virology* 2008;376:429–435.
35. Flaujac C, Boukour S, and Cramer-Bordé E. Platelets and viruses: an ambivalent relationship. *Cell Mol Life Sci* 2010;67:545–556.
36. Flaumenhaft R, and Sharda A. The life cycle of platelet granules. *F1000 Res* 2018;7:236.
37. Friedman EA, Ogletree ML, Haddad EV, and Boutaud O. Understanding the role of prostaglandin E2 in regulating human platelet activity in health and disease. *Thromb Res* 2015;136:493–503.
38. Furuta T, Murao LA, Lan NTP, *et al.* Association of mast cell-derived VEGF and proteases in dengue shock syndrome. *PLoS Negl Trop Dis* 2012;6:e1505.
39. Gubler DJ. Epidemic dengue/dengue hemorrhagic fever as a public health, social and economic problem in the 21st century. *Trends Microbiol* 2002;10:100–103.
40. Guerrero CD, Arrieta AF, Ramirez ND, *et al.* High plasma levels of soluble ST2 but not its ligand IL-33 is associated with severe forms of pediatric dengue. *Cytokine* 2013;61: 766–771.
41. Gupalo E, Kuk C, Qadura M, Buriachkovskaia L, and Othman M. Platelet–adenovirus vs. inert particles interaction: effect on aggregation and the role of platelet membrane receptors. *Platelets* 2013;24:383–391.
42. Guy B, Guirakhoo F, Barban V, Higgs S, Monath TP, and Lang J. Preclinical and clinical development of YFV 17D-based chimeric vaccines against dengue, West Nile and Japanese encephalitis viruses. *Vaccine* 2010;28:632–649.
43. Hadinegoro SR, Arredondo-García JL, Capeding MR, *et al.* Efficacy and long-term safety of a dengue vaccine in regions of endemic disease. *N Engl J Med* 2015;373: 1195–1206.
44. Halstead SB, Shotwell H, and Casals J. Studies on the pathogenesis of dengue infection in monkeys. I. clinical laboratory responses to primary infection. *J Infect Dis* 1973;128:7–14.
45. Kimura R and Hotta S. Studies on dengue fever (VI). On the inoculation of dengue virus into mice. *Nippom Igaku* 1944;3379:629–633.
46. Hsu AYH, Wu SR, Tsai JJ, *et al.* Infectious dengue vesicles derived from CD61+ cells in acute patient plasma exhibited a diaphanous appearance. *Sci Rep* 2015;5:17990.
47. Isakari Y, Sogo S, Ishida T, *et al.* Gene expression analysis during platelet-like particle production in phorbol myristate acetate-treated MEG-01 cells. *Biol Pharm Bull* 2009;32:354–358.
48. Jessie K, Fong MY, Devi S, Lam SK, and Wong KT. Localization of dengue virus in naturally infected human tissues, by immunohistochemistry and in situ hybridization. *J Infect Dis* 2004;189:1411–1418.
49. Kamau E, Takhampunya R, Li T, *et al.* Dengue virus infection promotes translocation of high mobility group box 1 protein from the nucleus to the cytosol in dendritic cells, upregulates cytokine production and modulates virus replication. *J Gen Virol* 2009;90:1827–1835.
50. Kar M, Singla M, Chandele A, Kabra SK, Lodha R, and Medigeshi GR. Dengue virus entry and replication does not lead to productive infection in platelets. *Open Forum Infect Dis* 2017;4:ofx051.
51. Kasirer-Friede A, Garraud O, Li W, Hottz ED, Bozza FA, and Bozza PT. Platelets in immune Response to virus and immunopathology of viral infections. *Front Med (Lausanne)* 2018;5:121.
52. Khan Assir MZ, Kamran U, Ahmad HI, *et al.* Effectiveness of platelet transfusion in dengue Fever: a randomized controlled trial. *Transfus Med Hemother* 2013;40:362–368.
53. Kirkpatrick BD, Whitehead SS, Pierce KK, *et al.* The live attenuated dengue vaccine TV003 elicits complete protection against dengue in a human challenge model. *Sci Transl Med* 2016;8:330ra36.
54. Kumar V, Gupta K, Soneja M, and Biswas A. Intravenous immunoglobulin for severe thrombocytopenia in secondary dengue. *BMJ Case Rep* 2018;2018:bcr2018224542.
55. Lahon A, Arya RP, and Banerjee AC. Dengue virus dysregulates master transcription factors and PI3K/AKT/mTOR signaling pathway in megakaryocytes. *Front Cell Infect Microbiol* 2021;11:715208.
56. Lam PK, Ngoc T Van, Thu Thuy TT, *et al.* The value of daily platelet counts for predicting dengue shock

- syndrome: results from a prospective observational study of 2301 Vietnamese children with dengue. *PLoS Negl Trop Dis* 2017;11:e0005498.
57. Leon C, Dupuis A, Gachet C, and Lanza F. The contribution of mouse models to the understanding of constitutional thrombocytopenia. *Haematologica* 2016;101:896–908.
 58. Libraty DH, Endy TP, Houg H-SH, *et al.* Differing influences of virus burden and immune activation on disease severity in secondary dengue-3 virus infections. *J Infect Dis* 2002;185:1213–1221.
 59. Lin G-L, Chang H-H, Lien T-S, *et al.* Suppressive effect of dengue virus envelope protein domain III on megakaryopoiesis. *Virulence* 2017;8:1719–1731.
 60. Lindemann S, Tolley ND, Dixon DA, *et al.* Activated platelets mediate inflammatory signaling by regulated interleukin 1 β synthesis. *J Cell Biol* 2001;154:485–490.
 61. Lye DC, Archuleta S, Syed-Omar SF, *et al.* Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial. *Lancet (London, England)* 2017;389:1611–1618.
 62. Lye DC, Lee VJ, Sun Y, and Leo YS. Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adults with acute uncomplicated dengue infection. *Clin Infect Dis* 2009;48:1262–1265.
 63. Machlus KR, and Italiano JE. The incredible journey: from megakaryocyte development to platelet formation. *J Cell Biol* 2013;201:785–796.
 64. Mangione JNA, Huy NT, Lan NTP, *et al.* The association of cytokines with severe dengue in children. *Trop Med Health* 2014;42:137–144.
 65. Manne BK, Xiang SC, and Rondina MT. Platelet secretion in inflammatory and infectious diseases. *Platelets* 2017;28:155.
 66. Masri MF Bin, Mantri CK, Rathore APS, and John ALS. Peripheral serotonin causes dengue virus-induced thrombocytopenia through 5HT₂ receptors. *Blood* 2019;133:2325–2337.
 67. de Mast Q, and de Groot PG. Serotonin, key to thrombocytopenia in dengue?. *Blood* 2019;133:2249–2250.
 68. Matattal KA, Jeong M, Chen S, *et al.* Chronic infection depletes hematopoietic stem cells through stress-induced terminal differentiation. *Cell Rep* 2016;17:2584–2595.
 69. Maugeri N, Campana L, Gavina M, *et al.* Activated platelets present high mobility group box 1 to neutrophils, inducing autophagy and promoting the extrusion of neutrophil extracellular traps. *J Thromb Haemost* 2014;12:2074–2088.
 70. Miagostovich MP, Ramos RG, Nicol AF, *et al.* Retrospective study on dengue fatal cases. *Clin Neuropathol* 1997;16:204–208.
 71. Michels M, Alisjahbana B, de Groot PG, *et al.* Platelet function alterations in dengue are associated with plasma leakage. *Thromb Haemost* 2014;112:352–362.
 72. Morales-Mantilla DE, and King KY. The role of interferon-gamma in hematopoietic stem cell development, homeostasis, and disease. *Curr Stem Cell Rep* 2018;4:264.
 73. Motulsky AG. Platelet agglutination by Influenza virus. *Clin Res Proc* 1953;1:100.
 74. Nascimento EJM, Hottz ED, Garcia-Bates TM, Bozza F, Marques ETA, and Barratt-Boyes SM. Emerging concepts in dengue pathogenesis: interplay between plasmablasts, platelets, and complement in triggering vasculopathy. *Crit Rev Immunol* 2014;34:227–240.
 75. Nelson ER, and Bierman HR. Dengue fever: a thrombocytopenic disease?. *JAMA* 1964;190:99–103.
 76. Noisakran S, Onlamoon N, Hsiao HM, *et al.* Infection of bone marrow cells by dengue virus *in vivo*. *Exp Hematol* 2012;40:250.
 77. Núñez-Avellaneda D, Mosso-Pani M, Sánchez-Torres L, Castro-Mussot M, la Peña NC, and Salazar M. Dengue virus induces the release of sCD40L and changes in levels of membranal CD42b and CD40L molecules in human platelets. *Viruses* 2018;10:357.
 78. Ogura M, Morishima Y, Ohno R, *et al.* Establishment of a novel human megakaryoblastic leukemia cell line, MEG-01, with positive philadelphia chromosome. *Blood* 1985;66:1384–1392.
 79. Oishi K, Inoue S, Cinco MTDD, *et al.* Correlation between increased platelet-associated IgG and thrombocytopenia in secondary dengue virus infections. *J Med Virol* 2003;71:259–264.
 80. Ojha A, Nandi D, Batra H, *et al.* Platelet activation determines the severity of thrombocytopenia in dengue infection. *Sci Rep* 2017;7:41697.
 81. Ong SP, Lee LM, Leong YFI, Ng ML, and Chu JJH. Dengue virus infection mediates HMGB1 release from monocytes involving PCAF acetylase complex and induces vascular leakage in endothelial cells. *PLoS One* 2012;7:e41932.
 82. Onlamoon N, Noisakran S, Hsiao HM, *et al.* Dengue virus - Induced hemorrhage in a nonhuman primate model. *Blood* 2010;115:1823–1834.
 83. Pascutti MF, Erkelens MN, and Nolte MA. Impact of viral infections on hematopoiesis: from beneficial to detrimental effects on bone marrow output. *Front Immunol* 2016;7(SEP):364.
 84. Perdomo-Celis F, Romero F, Salgado DM, *et al.* Identification and characterization at the single-cell level of cytokine-producing circulating cells in children with dengue. *J Infect Dis* 2018;217:1472–1480.
 85. Piguet PF, Vesin C, and Da Kan C. Activation of Platelet Caspases by TNF and its consequences for kinetics. *Cytokine* 2002;18:222–230.
 86. Pothapregada S, Kamalakannan B, and Thulasingam M. Role of platelet transfusion in children with bleeding in dengue fever. *J Vector Borne Dis* 2015;52:304–308.
 87. Putintseva E, Vega G, and Fernández L. Alterations in thrombopoiesis in patients with thrombocytopenia produced by dengue hemorrhagic fever. *Nouv Rev Fr Hematol* 1986;28:269–273.
 88. Quirino-Teixeira AC, Andrade FB, Pinheiro MBM, Rozini SV, and Hottz ED. Platelets in dengue infection: more than a numbers game. *Platelets* 2022;33:176–183.
 89. Raadsen M, Du Toit J, Langerak T, van Bussel B, van Gorp E, and Goeijenbier M. Thrombocytopenia in virus infections. *J Clin Med* 2021;10:877.
 90. Rajapakse S, de Silva NL, Weeratunga P, Rodrigo C, and Fernando SD. Prophylactic and therapeutic interventions for bleeding in dengue: a systematic review. *Trans R Soc Trop Med Hyg* 2017;111:433–439.
 91. Rathore APS, Mantri CK, Aman SAB, *et al.* Dengue virus-elicited tryptase induces endothelial permeability and shock. *J Clin Invest* 2019;129:4180–4193.

92. Renard N, Nooijen PTGA, Schalkwijk L, *et al.* VWF release and platelet aggregation in human melanoma after perfusion with TNF α . *J Pathol* 1995;176:279–287.
93. Rivadeneyra L, Pozner RG, Meiss R, Fondevila C, Gómez RM, and Schattner M. Poly (I:C) downregulates platelet production and function through type I interferon. *Thromb Haemost* 2015;114:982–993.
94. Robert A, Cortin V, Garnier A, Pineault N. Megakaryocyte and platelet production from human cord blood stem cells. *Methods Mol Biol* 2012;788:219–247.
95. Rodenhuis-Zybert IA, Schaar HM Van Der, Voorham JMDS, *et al.* Immature dengue virus: a veiled pathogen?. *PLoS Pathog* 2010;6:e1000718.
96. Rouhiainen A, Imai S, Rauvala H, and Parkkinen J. Occurrence of amphoterin (HMG1) as an endogenous protein of human platelets that is exported to the cell surface upon platelet activation. *Thromb Haemost* 2000; 84:1087–1094.
97. Sabin AB, and Schlesinger RW. Production of immunity to dengue with virus modified by propagation in mice. *Science* (80-) 1945;101:640–642.
98. Schmid MA, Diamond MS, and Harris E. Dendritic cells in dengue virus infection: targets of virus replication and mediators of immunity. *Front Immunol* 2014;0:647.
99. Sim X, Poncz M, Gadue P, and French DL. Understanding platelet generation from megakaryocytes: implications for in vitro-derived platelets. *Blood* 2016;127:1227–1233.
100. Simon AY, Sutherland MR, and Pryzdial ELG. Dengue virus binding and replication by platelets. *Blood* 2015; 126:378–385.
101. Sosman JA, Verma A, Moss S, *et al.* Interleukin 10-induced thrombocytopenia in normal healthy adult volunteers: evidence for decreased platelet production. *Br J Haematol* 2000;111:104–111.
102. Srikiatkhachorn A, Mathew A, and Rothman AL. Immune-mediated cytokine storm and its role in severe dengue. *Semin Immunopathol* 2017;39:563–574.
103. Suharti C, van Gorp ECM, Dolmans WM V, *et al.* Cytokine patterns during dengue shock syndrome. *Eur Cytokine Netw* 14:172–177.
104. Sung P-S, and Hsieh S-L. C-type lectins and extracellular vesicles in virus-induced NETosis. *J Biomed Sci* 2021; 28:46.
105. Sung PS, and Hsieh SL. CLEC2 and CLEC5A: pathogenic Host Factors in Acute Viral Infections. *Front Immunol* 2019;10:2867.
106. Takeuchi K, Satoh M, Kuno H, Yoshida T, Kondo H, and Takeuchi M. Platelet-like particle formation in the human megakaryoblastic leukaemia cell lines, MEG-01 and MEG-01s. *Br J Haematol* 1998;100:436–444.
107. Thakur P, Chakravarti A, Aggarwal S, Uppal B, and Bhalla P. Elevated levels of vascular endothelial growth factor in adults with severe dengue infection. *Virus Dis* 2016;27:48–54.
108. Thomas L, Kaidomar S, Kerob-Bauchet B, *et al.* Prospective observational study of low thresholds for platelet transfusion in adult dengue patients. *Transfusion* 2009;49: 1400–1411.
109. Thomas SJ, and Yoon IK. A review of Dengvaxia®: development to deployment. *Hum Vaccines Immunother* 2019;15:2295–2314.
110. Thon JN, Peters CG, Machlus KR, *et al.* T granules in human platelets function in TLR9 organization and signaling. *J Cell Biol* 2012;198:561–574.
111. Vinholt PJ, Frederiksen H, Hvas A-M, Sprogøe U, and Nielsen C. Measurement of platelet aggregation, independently of patient platelet count: a flow-cytometric approach. *J Thromb Haemost* 2017;15:1191–1202.
112. Vogt MB, Lahon A, Arya RP, Clinton JLS, and Rico-Hesse R. Dengue viruses infect human megakaryocytes, with probable clinical consequences. *PLoS Negl Trop Dis* 2019;13:e0007837.
113. Wan SW, Yang YW, Chu YT, *et al.* Anti-dengue virus nonstructural protein 1 antibodies contribute to platelet phagocytosis by macrophages. *Thromb Haemost* 2016; 115:646–656.
114. Weiss HJ, and Halstead SB. Studies of hemostasis in Thai hemorrhagic fever. *J Pediatr* 1965;66:918–926.
115. Whitehorn J, Rodriguez Roche R, Guzman MG, *et al.* Prophylactic platelets in dengue: survey responses highlight lack of an evidence base. *PLoS Negl Trop Dis* 2012; 6:e1716.
116. WHO. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva, Switzerland, 2009.
117. Wilder-Smith A. Moving forward with Takeda's live chimeric tetravalent dengue vaccine. *Lancet Infect Dis* 2017;17:566–568.
118. Yang H, Wang H, Chavan SS, and Andersson U. High mobility group box protein 1 (HMGB1): the prototypical endogenous danger molecule. *Mol Med* 2015; 21(Suppl 1): S6–S12.
119. Pan American Health Organization. Epidemiological Update Dengue. Year of report Total of dengue cases proportion of severe dengue cases. Washington, DC: PAHO/WHO, 2020.

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