



## Powering IFN-α Research with Ultra-Sensitive Simoa® Technology

Type 1 Interferons (IFNs) are a family of cytokines that play a central role in orchestrating the immune response to viral infections. Among them, IFN-α is the most studied subclass, comprising of 13 subtypes. These IFN-α subtypes are low-abundance yet highly potent proteins. Dysregulated IFN-α levels can adversely affect human health and have been implicated in the pathogenesis of various autoimmune conditions, as well as correlated with more severe disease outcomes. IFN-α holds significant promise as a biomarker for diagnosing, stratifying, and monitoring diseases, as well as a target for therapeutic approaches.

A critical aspect of this promise is the ability to measure IFN-α in blood, which has long been sought after and has only recently become possible with the advent of ultra-sensitive technologies such as the Simoa® digital immunoassay. Since its launch in 2016, Simoa® technology has been actively used in numerous studies related to IFN-α, as evidenced by over 80 peer-reviewed publications included in this brief, which have generated revolutionary insights into IFN-α biology and its clinical applications.

These studies employed various assays for IFN-α measurement, including the catalogued Simoa® IFN-α Advantage and Custom Homebrew Assays measuring either specific IFN-α subtypes or total IFN-α of all subtypes. Quanterix now offers the new Simoa® IFN-α Multi-Subtype (MS) Advantage PLUS (#103836) for ultra-sensitive measurement of total IFN-α.

### A sampling of recent publications include:

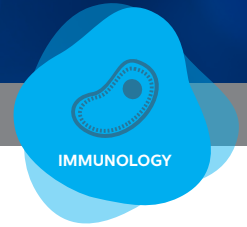
Publication	Assay Type
<b>COVID-19</b>	
Dissecting human population variation in single-cell responses to SARS-CoV-2. <i>Nature</i> . 2023;621(7977):120-128. doi:10.1038/s41586-023-06422-9	Homebrew
More rapid blood interferon α2 decline in fatal versus surviving COVID-19 patients. <i>Front Immunol</i> . 2023;14:1250214. Published 2023 Nov 21. doi:10.3389/fimmu.2023.1250214	Kit
Defective activation and regulation of type I interferon immunity is associated with increasing COVID-19 severity. <i>Nat Commun</i> . 2022;13(1):7254. Published 2022 Nov 25. doi:10.1038/s41467-022-34895-1	Homebrew - MS Kit
Lee D, Le Pen J, Yatim A, et al. Inborn errors of OAS-RNase L in SARS-CoV-2-related multisystem inflammatory syndrome in children. <i>Science</i> . 2023;379(6632):eabo3627. doi:10.1126/science.abo3627	Kit
Identification of bronchoalveolar and blood immune-inflammatory biomarker signature associated with poor 28-day outcome in critically ill COVID-19 patients. <i>Sci Rep</i> . 2022;12(1):9502. Published 2022 Jun 9. doi:10.1038/s41598-022-13179-0	Kit



Publication	Assay Type
<p>Plasma Exchange to Rescue Patients with Autoantibodies Against Type I Interferons and Life-Threatening COVID-19 Pneumonia. <i>J Clin Immunol.</i> 2021;41(3):536-544. doi:10.1007/s10875-021-00994-9</p>	Kit
<p>Inflammatory profiles across the spectrum of disease reveal a distinct role for GM-CSF in severe COVID-19. <i>Sci Immunol.</i> 2021;6(57):eabg9873. doi:10.1126/sciimmunol.abg9873</p>	Kit
<p>Polyclonal expansion of TCR Vbeta 21.3+ CD4+ and CD8+ T cells is a hallmark of Multisystem Inflammatory Syndrome in Children. <i>Sci Immunol.</i> 2021;6(59):eabh1516. doi:10.1126/sciimmunol.abh1516</p>	Kit
<p>Distinct cytokine profiles associated with COVID-19 severity and mortality. <i>J Allergy Clin Immunol.</i> 2021;147(6):2098-2107. doi:10.1016/j.jaci.2021.03.047</p>	Kit
<p>Systems vaccinology of the BNT162b2 mRNA vaccine in humans. <i>Nature.</i> 2021;596(7872):410-416. doi:10.1038/s41586-021-03791-x</p>	Kit
<p>Early nasal type I IFN immunity against SARS-CoV-2 is compromised in patients with autoantibodies against type I IFNs. <i>J Exp Med.</i> 2021;218(10):e20211211. doi:10.1084/jem.20211211</p>	Kit
<p>Seroconversion in septic ICU patients presenting with COVID-19: necessary but not sufficient. <i>Arch Med Res.</i> 2021;52(8):850-857. doi:10.1016/j.arcmed.2021.08.005</p>	Kit
<p>Release of infectious virus and cytokines in nasopharyngeal swabs from individuals infected with non-alpha or alpha SARS-CoV-2 variants: an observational retrospective study. <i>EBioMedicine.</i> 2021;73:103637. doi:10.1016/j.ebiom.2021.103637</p>	Homebrew
<p>Monoclonal antibody-mediated neutralization of SARS-CoV-2 in an IRF9-deficient child. <i>Proc Natl Acad Sci U S A.</i> 2021;118(45):e2114390118. doi:10.1073/pnas.2114390118</p>	Kit
<p>Type I IFN immunoprofiling in COVID-19 patients. <i>J Allergy Clin Immunol.</i> 2020;146(1):206-208.e2. doi:10.1016/j.jaci.2020.04.029</p>	Kit
<p>A dynamic COVID-19 immune signature includes associations with poor prognosis. <i>Nat Med.</i> 2020;26(10):1623-1635. doi:10.1038/s41591-020-1038-6</p>	Homebrew
<p>Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. <i>Science.</i> 2020;370(6515):eabd4570. doi:10.1126/science.abd4570</p>	Kit
<p>Autoantibodies against type I IFNs in patients with life-threatening COVID-19. <i>Science.</i> 2020;370(6515):eabd4585. doi:10.1126/science.abd4585</p>	Kit
<p>Type-I Interferon assessment in 45 minutes using the FilmArray® PCR platform in SARS-CoV-2 and other viral infections. <i>Eur J Immunol.</i> 2021;51(4):989-994. doi:10.1002/eji.202048978</p>	Kit



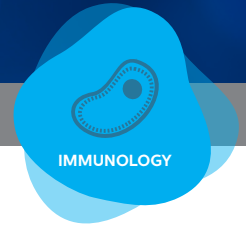
Publication	Assay Type
<b>Systemic Lupus Erythematosus (SLE)</b>	
Microfibrillar-associated protein 4 interaction with inflammation and clinical characteristics in neuropsychiatric systemic lupus erythematosus. <i>Front Lupus</i> . 2024;2:1386256.	Kit
Low CD4 + T cell count is related to specific anti-nuclear antibodies, IFNα protein positivity and disease activity in systemic lupus erythematosus pregnancy. <i>Arthritis Res Ther</i> . 2024;26(1):65. Published 2024 Mar 9. doi:10.1186/s13075-024-03301-0	Kit
Type I interferon blockade with anifrolumab in patients with systemic lupus erythematosus modulates key immunopathological pathways in a gene expression and proteomic analysis of two phase 3 trials. <i>Ann Rheum Dis</i> . Published online May 18, 2024. doi:10.1136/ard-2023-225445	Kit
Inactive disease in patients with lupus is linked to autoantibodies to type I interferons that normalize blood IFNα and B cell subsets. <i>Cell Rep Med</i> . 2023;4(1):100894. doi:10.1016/j.xcrm.2022.100894	Homebrew Kit - MS
Low-density granulocytes are related to shorter pregnancy duration but not to interferon alpha protein blood levels in systemic lupus erythematosus. <i>Arthritis Res Ther</i> . 2023;25(1):107. Published 2023 Jun 22. doi:10.1186/s13075-023-03092-w	Kit
Juvenile Neuropsychiatric Systemic Lupus Erythematosus: Identification of Novel Central Neuroinflammation Biomarkers. <i>J Clin Immunol</i> . 2023;43(3):615-624. doi:10.1007/s10875-022-01407-1	Homebrew
Serum IFNα2 levels are associated with disease activity and outperform IFN-I gene signature in a longitudinal childhood-onset SLE cohort. <i>Rheumatology (Oxford)</i> . 2023;62(8):2872-2879. doi:10.1093/rheumatology/keac698	Kit
Phase 3, multicentre, randomised, placebo-controlled study evaluating the efficacy and safety of ustekinumab in patients with systemic lupus erythematosus. <i>Ann Rheum Dis</i> . Published online July 7, 2022. doi:10.1136/ard-2022-222858	Kit
Activated low-density granulocytes in peripheral and intervillous blood and neutrophil inflammation in placentas from SLE pregnancies. <i>Lupus Sci Med</i> . 2021;8(1):e000463. doi:10.1136/lupus-2020-000463	Kit
Phase 1 study in healthy participants of the safety, pharmacokinetics, and pharmacodynamics of enpatoran (M5049), a dual antagonist of toll-like receptors 7 and 8. <i>Pharmacol Res Perspect</i> . 2021;9(5):e00842. doi:10.1002/prp2.842	Homebrew
S95021, a novel selective and pan-neutralizing anti interferon alpha (IFN-α) monoclonal antibody as a candidate treatment for selected autoimmune rheumatic diseases. <i>J Transl Autoimmun</i> . 2021;4:100093. Published 2021 Mar 1. doi:10.1016/j.jtauto.2021.100093	Homebrew - MS
Modulation of Cardiometabolic Disease Markers by Type I Interferon Inhibition in Systemic Lupus Erythematosus. <i>Arthritis Rheumatol</i> . 2021;73(3):459-471. doi:10.1002/art.41518	Kit



Publication	Assay Type
Control of TLR7-mediated type I IFN signaling in pDCs through CXCR4 engagement-A new target for lupus treatment. <i>Sci Adv.</i> 2019;5(7):eaav9019. Published 2019 Jul 10. doi:10.1126/sciadv.aav9019	Homebrew
Circulating Interferon- $\alpha$ Measured With a Highly Sensitive Assay as a Biomarker for Juvenile Inflammatory Myositis Activity: Comment on the Article by Mathian et al. <i>Arthritis Rheumatol.</i> 2020;72(1):195-197. doi:10.1002/art.41096	Homebrew
Ultrasensitive serum interferon- $\alpha$ quantification during SLE remission identifies patients at risk for relapse. <i>Ann Rheum Dis.</i> 2019;78(12):1669-1676. doi:10.1136/annrheumdis-2019-215571	Kit
Monitoring Disease Activity in Systemic Lupus Erythematosus With Single-Molecule Array Digital Enzyme-Linked Immunosorbent Assay Quantification of Serum Interferon- $\alpha$ . <i>Arthritis Rheumatol.</i> 2019;71(5):756-765. doi:10.1002/art.40792	Kit
<b>Dermatomyositis</b>	
IFN- $\beta$ plasmatic levels are best predictors of muscle disease activity than IFN- $\alpha$ in a longitudinal cohort of patients with juvenile dermatomyositis. Preprint. Published November 14, 2023. Available at: <a href="https://doi.org/10.21203/rs.3.rs-3582695/v1">https://doi.org/10.21203/rs.3.rs-3582695/v1</a> .	Homebrew
Osteonecrosis in patients with juvenile dermatomyositis: is it associated with anti-MDA5 autoantibody?. <i>Rheumatology (Oxford).</i> 2023;62(8):e242-e245. doi:10.1093/rheumatology/keac696	Homebrew
JAK inhibitors are effective in a subset of patients with juvenile dermatomyositis: a monocentric retrospective study. <i>Rheumatology (Oxford).</i> 2021;60(12):5801-5808. doi:10.1093/rheumatology/keab116	Homebrew
Onset and Relapse of Juvenile Dermatomyositis Following Asymptomatic SARS-CoV-2 Infection. <i>J Clin Immunol.</i> 2022;42(1):25-27. doi:10.1007/s10875-021-01119-y	Homebrew
Inhibition of IFN $\alpha$ secretion in cells from patients with juvenile dermatomyositis under TBK1 inhibitor treatment revealed by single-molecular assay technology. <i>Rheumatology (Oxford).</i> 2020;59(5):1171-1174. doi:10.1093/rheumatology/kez508	Homebrew
A child with severe juvenile dermatomyositis treated with ruxolitinib. <i>Brain.</i> 2018;141(11):e80. doi:10.1093/brain/awy255	Homebrew
JAK inhibitor improves type I interferon induced damage: proof of concept in dermatomyositis. <i>Brain.</i> 2018;141(6):1609-1621. doi:10.1093/brain/awy105	Homebrew
<b>Other Infectious Disease</b>	
Single-cell landscape of peripheral immune responses to fatal SFTS. <i>Cell Rep.</i> 2021;37(8):110039. doi:10.1016/j.celrep.2021.110039	Kit
Decreased Type I Interferon Production by Plasmacytoid Dendritic Cells Contributes to Severe Dengue. <i>Front Immunol.</i> 2020;11:605087. Published 2020 Dec 17. doi:10.3389/fimmu.2020.605087	Homebrew



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Systems Biology Methods Applied to Blood and Tissue for a Comprehensive Analysis of Immune Response to Hepatitis B Vaccine in Adults. <i>Front Immunol.</i> 2020;11:580373. Published 2020 Nov 4. doi:10.3389/fimmu.2020.580373	Kit
A Single and Multiple Ascending Dose Study of Toll-Like Receptor 7 Agonist (R07020531) in Chinese Healthy Volunteers. <i>Clin Transl Sci.</i> 2020;13(5):985-993. doi:10.1111/cts.12791	Kit
Plasmacytoid dendritic cells sense HIV replication before detectable viremia following treatment interruption. <i>J Clin Invest.</i> 2020;130(6):2845-2858. doi:10.1172/JCI130597	Kit
TLR7 dosage polymorphism shapes interferogenesis and HIV-1 acute viremia in women. <i>JCI Insight.</i> 2020;5(12):e136047. Published 2020 Jun 18. doi:10.1172/jci.insight.136047	Kit
A randomized trial of vorinostat with treatment interruption after initiating antiretroviral therapy during acute HIV-1 infection. <i>J Virus Erad.</i> 2020;6(3):100004. Published 2020 Jul 18. doi:10.1016/j.jve.2020.100004	Kit
Plasma Type I IFN Protein Concentrations in Human Tuberculosis. <i>Front Cell Infect Microbiol.</i> 2019;9:296. Published 2019 Aug 22. doi:10.3389/fcimb.2019.00296	Homebrew
Plasmacytoid dendritic cells control dengue and Chikungunya virus infections via IRF7-regulated interferon responses. <i>Elife.</i> 2018;7:e34273. Published 2018 Jun 19. doi:10.7554/eLife.34273	Homebrew
Mitochondrial double-stranded RNA triggers antiviral signalling in humans. <i>Nature.</i> 2018;560(7717):238-242. doi:10.1038/s41586-018-0363-0	Homebrew
<b>Other Immunology, Inflammation and Autoimmunity</b>	
Interferon and interferon-induced cytokines as markers of impending clinical progression in ANA+ individuals without a systemic autoimmune rheumatic disease diagnosis. <i>Arthritis Res Ther.</i> 2023;25(1):21. Published 2023 Feb 10. doi:10.1186/s13075-023-02997-w	Kit
Central Role of Macrophages and Nucleic Acid Release in Myasthenia Gravis Thymus. <i>Ann Neurol.</i> 2023;93(4):643-654. doi:10.1002/ana.26590	Homebrew
Interferon signature in giant cell arteritis aortitis. <i>J Autoimmun.</i> 2022;127:102796. doi:10.1016/j.jaut.2022.102796	Kit
Pulmonary Alveolar Proteinosis and Multiple Infectious Diseases in a Child with Autosomal Recessive Complete IRF8 Deficiency. <i>J Clin Immunol.</i> 2022;42(5):975-985. doi:10.1007/s10875-022-01250-4	Kit
High-efficiency nonviral CRISPR/Cas9-mediated gene editing of human T cells using plasmid donor DNA. <i>J Exp Med.</i> 2022;219(5):e20211530. doi:10.1084/jem.20211530	Kit
A partial form of inherited human USP18 deficiency underlies infection and inflammation. <i>J Exp Med.</i> 2022;219(4):e20211273. doi:10.1084/jem.20211273	Kit



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<p><b>Interferon-<math>\alpha</math>-mediated therapeutic resistance in early rheumatoid arthritis implicates epigenetic reprogramming.</b>  <i>Ann Rheum Dis.</i> 2022;81(9):1214-1223. Published 2022 Aug 11. doi:10.1136/annrheumdis-2022-222370</p>	Homebrew
<p><b>Differential levels of IFN<math>\alpha</math> subtypes in autoimmunity and viral infection.</b>  <i>Cytokine.</i> 2021;144:155533. doi:10.1016/j.cyto.2021.155533</p>	Homebrew
<p><b>Depleting plasmacytoid dendritic cells reduces local type I interferon responses and disease activity in patients with cutaneous lupus.</b>  <i>Sci Transl Med.</i> 2021;13(595):eabf8442. doi:10.1126/scitranslmed.abf8442</p>	Kit
<p><b>Constitutive IFN<math>\alpha</math> Protein Production in Bats.</b>  <i>Front Immunol.</i> 2021;12:735866. Published 2021 Nov 1. doi:10.3389/fimmu.2021.735866</p>	Homebrew
<p><b>Positive Allosteric Modulation of A2AR Alters Immune Cell Responses and Ameliorates Psoriasis-Like Dermatitis in Mice.</b>  <i>J Invest Dermatol.</i> 2022;142(3 Pt A):624-632.e6. doi:10.1016/j.jid.2021.07.174</p>	Kit
<p><b>Differential Expression of Interferon-Alpha Protein Provides Clues to Tissue Specificity Across Type I Interferonopathies.</b>  <i>J Clin Immunol.</i> 2021;41(3):603-609. doi:10.1007/s10875-020-00952-x</p>	Homebrew
<p><b>Plasma interferon-alpha is associated with double-positivity for autoantibodies but is not a predictor of remission in early rheumatoid arthritis-a spin-off study of the NORD-STAR randomized clinical trial.</b>  <i>Arthritis Res Ther.</i> 2021;23(1):189. Published 2021 Jul 13. doi:10.1186/s13075-021-02556-1</p>	Homebrew
<p><b>A new molecular classification to drive precision treatment strategies in primary Sjögren's syndrome.</b>  <i>Nat Commun.</i> 2021;12(1):3523. Published 2021 Jun 10. doi:10.1038/s41467-021-23472-7</p>	Kit
<p><b>Serum interferon-<math>\alpha</math>2 measured by single-molecule array associates with systemic disease manifestations in Sjögren's syndrome.</b>  <i>Rheumatology (Oxford).</i> 2022;61(5):2156-2166. doi:10.1093/rheumatology/keab688</p>	Kit
<p><b>Local delivery of mRNA-encoded cytokines promotes antitumor immunity and tumor eradication across multiple preclinical tumor models.</b>  <i>Sci Transl Med.</i> 2021;13(610):eabc7804. doi:10.1126/scitranslmed.abc7804</p>	Kit
<p><b>Altered Immune Phenotypes and HLA-DQB1 Gene Variation in Multiple Sclerosis Patients Failing Interferon <math>\beta</math> Treatment.</b>  <i>Front Immunol.</i> 2021;12:628375. Published 2021 May 25. doi:10.3389/fimmu.2021.628375</p>	Homebrew
<p><b>Systemic Type I IFN Inflammation in Human ISG15 Deficiency Leads to Necrotizing Skin Lesions.</b>  <i>Cell Rep.</i> 2020;31(6):107633. doi:10.1016/j.celrep.2020.107633</p>	Kit
<p><b>Type I IFN is siloed in endosomes.</b>  <i>Proc Natl Acad Sci U S A.</i> 2020;117(30):17510-17512. doi:10.1073/pnas.1921324117</p>	Kit



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<b>Mutations in COPA lead to abnormal trafficking of STING to the Golgi and interferon signaling.</b> <i>J Exp Med.</i> 2020;217(11):e20200600. doi:10.1084/jem.20200600	Homebrew
<b>Innate immune stimulation of whole blood reveals IFN-1 hyper-responsiveness in type 1 diabetes.</b> <i>Diabetologia.</i> 2020;63(8):1576-1587. doi:10.1007/s00125-020-05179-4	Kit
<b>Inflammatory profiles relate to survival in subtypes of amyotrophic lateral sclerosis.</b> <i>Neurol Neuroimmunol Neuroinflamm.</i> 2020;7(3):e697. Published 2020 Mar 2. doi:10.1212/NXI.0000000000000697	Kit
<b>Risk factors associated with myasthenia gravis in thymoma patients: The potential role of thymic germinal centers.</b> <i>J Autoimmun.</i> 2020;106:102337. doi:10.1016/j.jaut.2019.102337	Homebrew
<b>Use of ruxolitinib in COPA syndrome manifesting as life-threatening alveolar haemorrhage.</b> <i>Thorax.</i> 2020;75(1):92-95. doi:10.1136/thoraxjnl-2019-213892	Homebrew
<b>Anti-MDA5 juvenile idiopathic inflammatory myopathy: a specific subgroup defined by differentially enhanced interferon-α signalling.</b> <i>Rheumatology (Oxford).</i> 2020;59(8):1927-1937. doi:10.1093/rheumatology/kez525	Homebrew
<b>PSMB10, the last immunoproteasome gene missing for PRAAS.</b> <i>J Allergy Clin Immunol.</i> 2020;145(3):1015-1017.e6. doi:10.1016/j.jaci.2019.11.024	Homebrew
<b>Interferon signature in patients with STAT1 gain-of-function mutation is epigenetically determined.</b> <i>Eur J Immunol.</i> 2019;49(5):790-800. doi:10.1002/eji.201847955	Homebrew
<b>Bloom syndrome protein restrains innate immune sensing of micronuclei by cGAS.</b> <i>J Exp Med.</i> 2019;216(5):1199-1213. doi:10.1084/jem.20181329	Homebrew
<b>Type I interferon in patients with systemic autoimmune rheumatic disease is associated with haematological abnormalities and specific autoantibody profiles.</b> <i>Arthritis Res Ther.</i> 2019;21(1):147. Published 2019 Jun 14. doi:10.1186/s13075-019-1929-4	Homebrew
<b>Plasma Neurofilament Light Chain Levels Are Associated With Cortical Hypometabolism in Alzheimer Disease Signature Regions.</b> <i>J Neuropathol Exp Neurol.</i> 2019;78(8):709-716. doi:10.1093/jnen/nlz054	Homebrew
<b>Neuromyelitis optica in patients with increased interferon alpha concentrations.</b> <i>Lancet Neurol.</i> 2020;19(1):31-33. doi:10.1016/S1474-4422(19)30445-4	Homebrew
<b>Development and Validation of an Ultrasensitive Single Molecule Array Digital Enzyme-linked Immunosorbent Assay for Human Interferon-α.</b> <i>J Vis Exp.</i> 2018;(136):57421. Published 2018 Jun 14. doi:10.3791/57421	Homebrew - MS
<b>Elevated Neopterin Levels Predict Early Death in Older Hip-fracture Patients.</b> <i>EBioMedicine.</i> 2017;26:157-164. doi:10.1016/j.ebiom.2017.11.003	Kit
<b>Detection of interferon alpha protein reveals differential levels and cellular sources in disease.</b> <i>J Exp Med.</i> 2017;214(5):1547-1555. doi:10.1084/jem.20161451	Homebrew - MS
<b>Type I interferon-mediated autoinflammation due to DNase II deficiency.</b> <i>Nat Commun.</i> 2017;8(1):2176. Published 2017 Dec 19. doi:10.1038/s41467-017-01932-3	Homebrew