Interferon-α Modulates the Host Glycosylation Machinery During Treated HIV Infection

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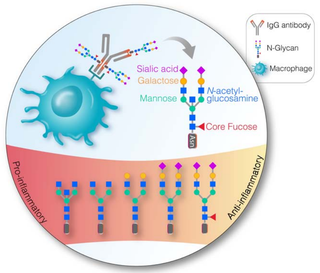
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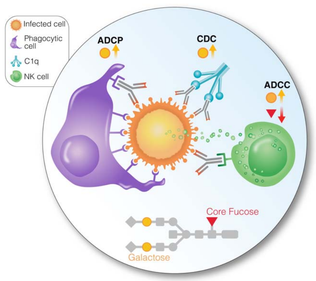
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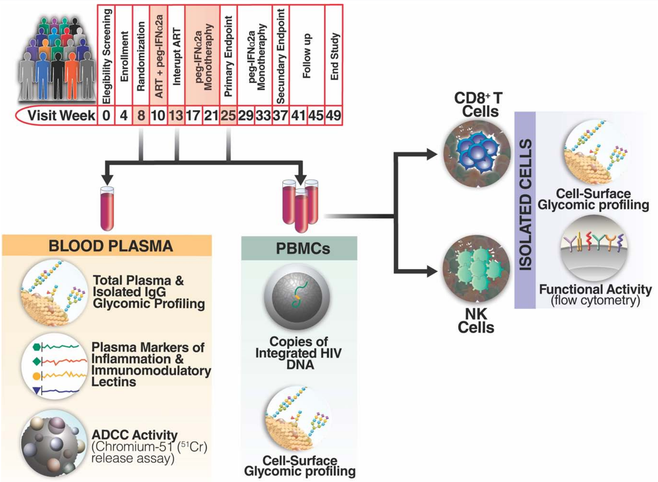
BACKGROUND

- Interferon-α (IFNα) therapy was associated with significant suppression of HIV viremia and reduction in levels of HIV DNA during suppressive antiretroviral therapy (ART).
- Cytokines modulate host glycosylation, and glycosylation plays a critical role in mediating several cellular processes and immunological functions including antibody-dependent cell-mediated cytotoxicity (ADCC), and anti-inflammatory activities. Nevertheless, the impact of IFNα on host glycosylation machinery remains unknown.





METHODS



RESULTS

Figure 1. Peg-IFNα2a treatment induces the proportion of the pro-inflammatory, bisected GlcNAc glycans on plasma IgG. (A) Violin plots of IgG glycan structures modulated by IFNα. ANOVA test. **(B-F)** Bar graphs of selected bisected IgG glycan structures modulated by IFNα. ANOVA test (Median ±Interquartile range). **(G)** Bisected GlcNAc glycans on total plasma glycoproteins. Wilcoxon signed-rank test (Median ±Interquartile range).

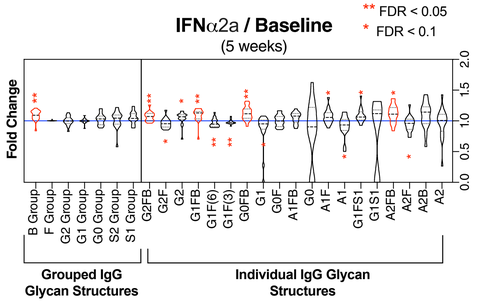


Figure 2. Peg-IFNα2a-mediated induction of the pro-inflammatory bisected GlcNAc on IgG associates with higher monocyte and macrophage activation/inflammation. (A-D) IFNα treatment induces the levels of sCD14, sCD163, IL-18, and reduces the levels of IL-10. **(E-G)** IFNα2-mediated induction of the pro-inflammatory bisected GlcNAc on IgG correlates with higher levels of IFNα2-mediated induction of markers of monocyte and macrophage activation/inflammation.

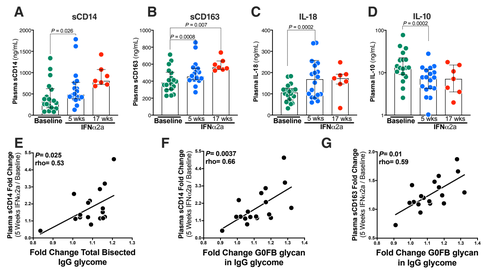


Figure 3. Interaction network of IFN-mediated modulation of the IgG glycomes, plasma inflammatory markers, and both CD8+ T and NK cell phenotypes. Circos plots describe the correlations between Peg-IFNα2a-mediated changes in the IgG glycomes, plasma markers, and **(A)** CD8+ T cell and **(B)** K652-stimulated NK cell phenotypes. Correlations connected the three domains are highlighted.

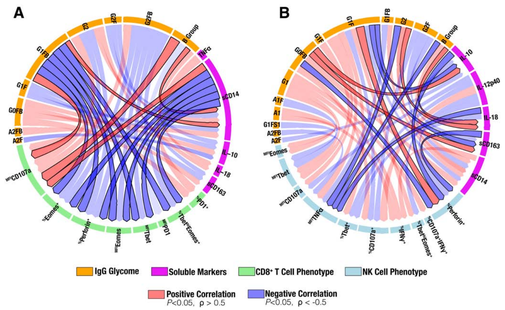
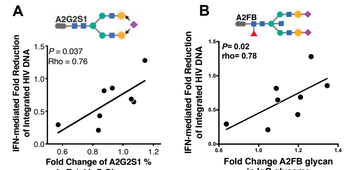


Figure 4. IFNα-mediated modulation of the IgG glycome correlates with IFN-mediated Reduction of Integrated HIV DNA. Spearman's rank correlation.



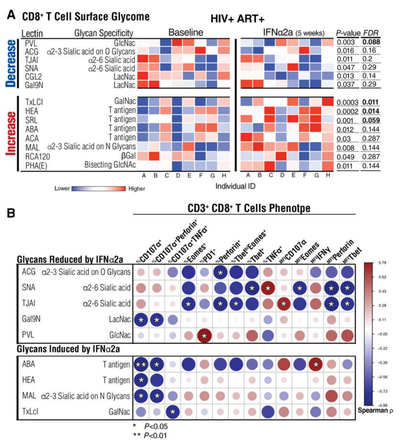


Figure 5. IFNα modulates CD8+ T cell-surface glycome. (A) Impact of Peg-IFNα2a treatment on CD8+ T cell surface glycomes. Wilcoxon signed-rank test. **(B)** Associations between IFNα2a-mediated changes on the CD8+ T cell-surface glycomes and CD8+ T cell phenotypes. Spearman's correlations.

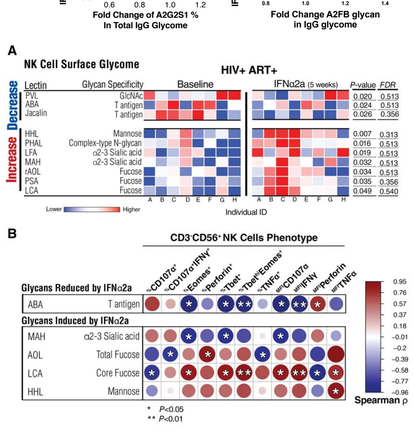


Figure 6. IFNα modulates NK cell-surface glycome. (A) Impact of Peg-IFNα2a treatment on NK cell surface glycomes. Wilcoxon signed-rank test. **(B)** Associations between IFNα2a-mediated changes on the NK cell glycomes and K652-stimulated NK cell phenotypes. Spearman's correlations.

CONCLUSIONS

- IFNα causes host glycomic alterations that are known to mediate inflammatory responses. These alterations are associated with mainly detrimental, but also beneficial, consequences of IFNα on innate and adaptive immune functions. Manipulating glycan-lectin interactions may represent a strategy to enhance the impact of IFNα on immunity while avoiding its detrimental side-effects.

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