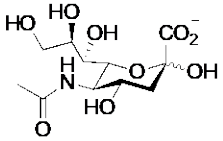
*From Laboratory of Experimental Pathology*

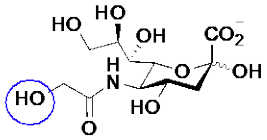
# Human species-specific loss of CMP-N-acetylneuraminic acid hydroxylase enhances atherosclerosis via intrinsic and extrinsic mechanisms

Human *CMAH* Pseudogenization

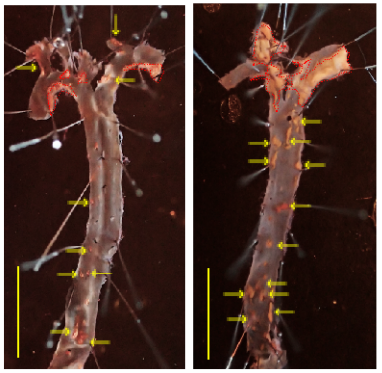


Neu5Ac

CMAH



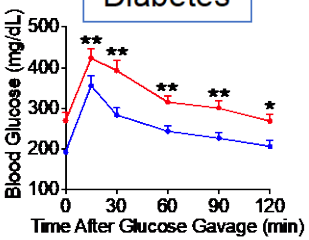
Neu5Gc



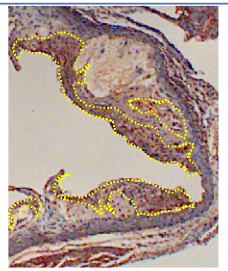
Neu5Gc Neu5Ac

WT Humanized Mice

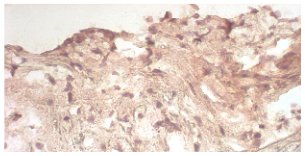
Diabetes

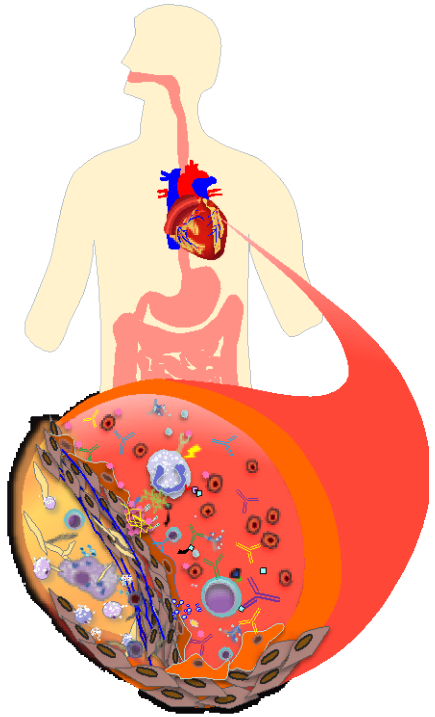



Hyper-Reactive Macrophage



Xenosialitis (Neu5Gc – anti-Neu5Gc antibodies)





This research was conducted at Varki lab, University of California, San Diego

Inactivation of the CMP-N-acetylneuraminic acid (Neu5Ac) hydroxylase (CMAH) occurred 2 to 3 million years ago in the hominin lineage, which is manifest as a human deficiency of the common mammalian sialic acid N-glycolylneuraminic acid (Neu5Gc).
This Neu5Gc loss contributes to atherosclerosis risk via intrinsic mechanisms such as up-regulated inflammatory response and hyperglycemia as well as extrinsic mechanisms such as red meat-derived Neu5Gc-induced xenosialitis.

References: Kawanishi et al., Proc Natl Acad Sci U S A. 2019; 116 : 16036-16045

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