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Principal Investigator: Frederic A. Troy II
Organization: University of California School of Medicine
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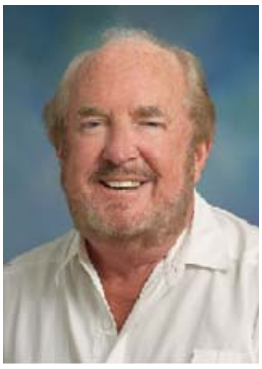
Grant Title: *"Functional Analyses of Polysialic Acid DP on Human Cancer Stem Cells"*



Objectives: Our initial objective was to determine the degree of polymerization (DP) of polySia chains on NCAM in stem cells and in cancers of the head and neck (H&N), and how the DP may correlate with the potential for metastatic invasion.
Methods used: We sought to use a new strategy we developed to accurately assess the DP of polySia chains on NCAM after their enzymatic release with Endo-β-galactosidase under non-hydrolytic conditions, as described in JBC (2005) 280; 38305-38316).

Results: Substantial progress was made in our aim to elucidate the role of sialic acids in adult guinea pig stem cells after neuronal differentiation of inner ear spiral ganglion neurons ***(Pub. #1)*.** Correlative studies related to our principle aim was made possible by Mizutani funding and acknowledged in publication. These include: (**Pub. #2**). (2015) ***"****LC-MS/MS Glycomic Analyses of Free and Conjugated Forms of the Sialic Acids, Neu5Ac, Neu5Gc and KDN in Human Throat Cancers"* (In Press; Glycobiology July 2015); (**Pub. #3**). (2015) *"Molecular Characterization and Expression Analyses of ST8Sia II and IV in Piglets During Postnatal Development: Lack of Correlation Between Transcription and Posttranslational Levels"*. (Submitted. July, 2015*);* ***(*Pub. #4*)***. (2015) "*3D Structural Conformation and Functional Domains of Polysialyltransferase ST8Sia IV Required for Polysialylation of Neural Cell Adhesion Molecules"*. Protein & Peptide Letters. **22***; 137-14;* **(Pub. #5***)* (2013) "*LC-MS/MS Quantification of Neu5Ac, Neu5Gc and KDN Levels in the Urine and Potential Relationship with Dietary Sialic Acid Intake and Disease in 3- to 5-year old Children"***.** (2013) Brit. Jour. Nutrition **5**; 1-10; **(Pub. #6**). (2014) "*Lactoferrin Promotes Early Brain Development and Cognition in Postnatal Piglets by Up-regulating the BDNF Signaling Pathway and Polysialylation"*. Molecular Neurobiology .DOI 10.1007/s12035-014-8856-9; **(Pub.#7).** **(**2014) *"Development of new population-averaged standard templates for spatial normalization and segmentation of MR images for postnatal piglet brains"*. Magnetic Resonance Imaging. http://dx.doi.org/10.1016j.mri.2014.08.036.

Discussion: The unexpected finding described in **Pub. #1** has provided a new source of adult neural stem cells for DP analyses. Because of difficulty in obtaining Endo-β-galactosidase for release of polySia chains from NCAM (V-Labs out of business), we initiated studies to analyze other endo-glycohydrolyases. Initial results of these on-going studies have now provided alternate ways to enzymatically release the polySia-N-linked oligosaccharide chains from NCAM. As noted in our 7 publications (below), Mizutani funding was instrumental in our completing the research and publication of correlative studies that complement our overarching goal of elucidating the molecular role of polysialic acid in stem cell, cancer and neurobiology.