The long island subsection
Of
The New York American chemical society

Proudly presents

Dr. Ruel Desamero,

from York College of CUNY, Department of Chemistry

Title of Talk: "Conformational Consequences and Structural Details of the Self-Assembly of $hIAPP_{22-29}$"

Synopsis: The octapeptide NFGAILSS ($hIAPP_{22-29}$), derived from human islet amyloid polypeptide, has been extensively used as a model system to study amyloid formation. However, despite being the target of numerous investigations, information describing specific molecular interactions and conformational details are still lacking in regard to aggregates formed by this peptide. We synthesized peptide analogs of $hIAPP_{22-29}$ and employed turbidity measurements in conjunction with FTIR, Raman and fluorescence spectroscopy along with computer modeling to investigate and probe the structure of aggregates formed by the NFGAILSS sequence. Our findings unambiguously indicate that, at neutral pH, $hIAPP_{22-29}$ self-assembles into a parallel β-sheet secondary structure in which the aromatic ring of Phe-23 engages in π-stacking interactions. Computational modeling confirms that of the possible ring stacking motifs (sandwich, parallel displaced, parallel staggered and T-shaped geometries) only a parallel displaced stacking arrangement can account for the observed vibrational modes in the Raman spectra. The amide I vibrational mode *ca.* 1655 cm^{-1} in the Raman spectra of aggregates from $hIAPP_{22-29}$ indicates the presence of a parallel β-sheet secondary structure. Fluorescence data also support these observations and point to the formation of excimers due to ring stacking. These observations are compared and contrasted to results obtained with amidated $hIAPP_{20-29}$ ($SNNFGAILSS-NH_2$) analogs that are only capable of forming amyloid composed of antiparallel β-sheets in which π-stacking interactions involving Phe-23 cannot occur. Consistent with this, the presence of an electron donating substituent on the aromatic ring of Phe-23 was found not to abolish the amyloidogenic potential of $hIAPP_{20-29}$ as it has previously been shown with $hIAPP_{22-29}$. Raman spectra of aggregates formed from $hIAPP_{20-29}$ were distinctly different from those of $hIAPP_{22-29}$ in the amide and ring mode vibrational regions and provide evidence of an antiparallel β-sheet structure. Finally, results from these investigations reveal that the $hIAPP_{22-29}$ sequence is sensitive to its chemical environment and can undergo "conformational switching" between parallel and antiparallel β-sheets in response to changes in pH. The ramifications of the above findings are discussed in the context of other amyloidogenic systems and full-length hIAPP.

All are welcome!

When: Thursday, April 4th, 2019

Where: Queensborough Community College, Science Building Rm S-112

Time: 5:30 p.m. – Social w/ Light Refreshments; 6:00 pm – Seminar Start

Directions: http://www.qcc.cuny.edu/about/driving.html

After Seminar Dinner: At a nearby restaurant, $25 per person.

American Chemical Society Long Island Subsection
http://www.newyorkacs.org/sub_island.php