

WINTER 2005 SEMINAR SERIES

F21C BIOPROCESSING & BIOSENSING CENTER

• DIVISION OF FOOD SYSTEMS & BIOENGINEERING •

PRESENTER

Dr. Michael R. Nichols, Assistant Professor, Department of Chemistry and Biochemistry, University of Missouri-St. Louis

TITLE

Amyloid- β Aggregates Formed at Polar-Nonpolar Interfaces Differ From Amyloid- β Protofibrils Produced in Aqueous Buffers

ABSTRACT

The deposition of aggregated amyloid- β (A β) peptides in the brain in the form of senile plaques is a pathological hallmark of Alzheimer's disease (AD). Several lines of evidence indicate that fibrillar and, in particular, soluble aggregates of these 40- and 42-residue peptides are important in the etiology of AD. Recent reports also stress that amyloid aggregates are polymorphic and that a single polypeptide can fold into multiple amyloid conformations. We have demonstrated that A β (1-40) in vitro can form soluble aggregates with predominant β -structures that differ in stability and morphology. One class of aggregates involved soluble A β protofibrils, prepared by vigorous overnight agitation of monomeric A β (1-40) in low ionic strength buffers. These aggregates were quite stable and disaggregated to only a limited extent on dilution. A second class of soluble A β aggregates was generated at nonpolar interfaces. Aggregation in a two-phase system of buffer over chloroform occurred more rapidly than in buffer alone. In buffered 2% hexafluoroisopropanol (HFIP), microdroplets of HFIP were formed and the half time for aggregation was less than 10 min. Like A β protofibrils, these interfacial aggregates showed increased thioflavin T fluorescence and were rich in β -structure by circular dichroism. However, electron microscopy and atomic force microscopy revealed very different morphologies. The HFIP aggregates formed initial globular clusters that progressed over several days to soluble fibrous aggregates. When diluted out of HFIP these aggregates initially were very unstable and disaggregated completely within 2 min. However, their stability increased as they progressed to fibers. It is important to determine whether similar interfacial A β aggregates are produced in vivo.

DATE • TIME • LOCATION

Tuesday, May 3, 4:00pm
Ag Eng Bldg 105 • Refreshments