Short Peptides as Inhibitors of Amyloid Aggregation

Bradley Neddenriep, Anastasia Calciano, Daniel Conti, Erin Sauve, Marissa Paterson, Edward Bruno and David A. Moffet*

Department of Chemistry and Biochemistry Loyola Marymount University 1 LMU Drive Los Angeles, CA 90045, USA

Abstract: The misfolding and aggregation of proteins into amyloid has been linked to a variety of age-related diseases. Aggregation of proteins, such as Aβ in Alzheimer’s disease and Islet Amyloid Polypeptide (IAPP, amylin) in type 2 diabetes, appears to lead to the formation of toxic assemblies. These assemblies range in size from small oligomers (2-8 proteins) to large fibrils (thousands of proteins). It remains unclear how these amyloidogenic proteins misfold and form toxic species, but growing evidence suggests that inhibiting the aggregation of these proteins could slow, if not prevent altogether, the progression of these diseases. We describe the use of small peptides (<43 amino acids) as inhibitors of amyloid-based aggregation. These peptides, often short complementary segments of the amyloid proteins, can be useful (i) for identifying the aggregation-prone regions of the amyloid proteins (ii) as models for drug discovery and (iii) as potential therapeutic agents themselves.

Keywords: Amyloid Inhibition, Peptide Libraries, Aβ, Amylin, IAPP.

INTRODUCTION

Many proteins are known to adopt unwanted, misfolded structures that can be linked to a variety of age-related diseases [1-3]. Proteins such as Islet Amyloid Polypeptide (IAPP, amylin) in type 2 diabetes and Aβ42 in Alzheimer’s disease are known to misfold and aggregate into toxic oligomers and fibers. In these amyloid diseases, proteins misfold and self-assemble into a variety of structures. It remains unknown if these misfolded proteins are the cause of their respective diseases or a side-effect. However, evidence is accumulating to suggest that the aggregation of amyloid proteins plays an important role in the development and progression of these diseases.

The amyloid diseases represent a serious threat to our overall global health. Within the United States, the economic and social costs associated with Alzheimer’s disease and type 2 diabetes have been well documented over the past decade. The Alzheimer’s Association estimates that 5.1 million Americans are currently afflicted with Alzheimer’s disease [4]. Likewise, the American Diabetes Association estimates that 23.6 million children and adults in the United States have diabetes [5]. Because the prevalence of these diseases increases with age, the number of people afflicted with Alzheimer’s disease and type 2 diabetes will increase as the population ages. If no treatments are found to slow these diseases, it is estimated that 11 to 16 million Americans will be afflicted with Alzheimer’s disease by 2050 [4] and as many as 100 million Americans could have diabetes by that time [6]. The economic costs of just these two amyloidogenic diseases is estimated to be more than $148 billion annually for Alzheimer’s disease and $174 billion for type 2 diabetes.

*Address correspondence to this author at the Department of Chemistry and Biochemistry Loyola Marymount University 1 LMU Drive Los Angeles, CA 90045, USA; Tel: 310-338-4400; Fax: 001-310-338-2905; E-mail: dmoffet@lmu.edu

While the amyloidogenic proteins differ in many ways (length, organismal localization, amino acid compositions), they all form well-ordered fibrils and appear to be toxic to living cells [7-14]. These similarities are not solely shared by naturally occurring proteins, but have been identified in designed proteins expressed in mammalian cells [15]. These results indicate that the formation of protein aggregates, whether they are small oligomers or large fibrils, plays a central role in cell toxicity and disease pathology. These studies suggest that the mechanism of this cellular toxicity is likely conserved from one amyloid protein to the next. These results raise the hope that if a strategy is uncovered to prevent amyloid formation for one disease, the same strategy may lead to therapies for many, if not all, of the remaining amyloid diseases.

Many strategies are currently being assessed for preventing the formation of amyloid and toxic oligomers. Some strategies rely on preventing the production of the amyloid protein in the first place (for instance, inhibiting γ-secretase activity in Aβ production). Some strategies rely on removing the amyloid protein after it has been produced (such as using antibodies to remove Aβ). Both of these strategies hold great potential for slowing and/or preventing the onset of amyloid-based diseases. However, it remains to be determined if the amyloid proteins themselves serve a useful purpose to the organism. There may be a benefit to having the protein that has not yet been determined. With this in mind, there have been some recent successes made in slowing the rate of aggregation of amyloid proteins without having to remove the protein entirely. Several classes of small molecules have been identified as showing some activity toward inhibiting the formation of amyloid. [16-27]. While small-molecule aggregation inhibitors have been reported, none have been developed into a clinically useful therapeutic.
Since 2002, we have seen a considerable increase in the number of reports identifying short peptides as inhibitors of amyloid formation. While none of these peptides have been developed into a therapeutic, the potential does exist. Unlike small-molecule inhibitors of amyloid aggregation, short peptides can yield information regarding the amyloid aggregates themselves. Many of the peptide inhibitors are truncated versions of the full-length amyloid proteins. By identifying the sequence regions that inhibit aggregation, we can infer that those are the regions responsible for driving amyloid aggregation. In this review, we will focus on the short peptide sequences comprised of naturally occurring amino acids that have been identified for their ability to inhibit the aggregation of the amyloidogenic proteins Aβ (Alzheimer’s disease) and IAPP (type 2 diabetes).

PEPTIDE INHIBITION OF ABETA AGGREGATION

Peptides showing an ability to inhibit the aggregation of Aβ can be organized into two major groups; rationally designed peptides (which are typically similar in sequence to that of wild-type Aβ) and randomly generated peptides (those which are identified from peptide libraries that may, or may not, show sequence similarity to wild-type Aβ). The advances made in molecular biology and biotechnology in the past decade have made it possible to construct and screen large peptide libraries to identify those sequences that interact with Aβ. These library-screening experiments, which were either impossible or impractical just a few years ago, have successfully identified several amyloid inhibitors.

Rationally Designed Peptide Inhibitors of Aβ Aggregation

The earliest attempts to identify Aβ aggregation inhibitors came from the sequence of Aβ itself (Table 1). Many of the first peptide inhibitors were designed to target the aggregation-prone hydrophobic core region of Aβ. This region (LVFFA) is considered by many to be the primary aggregation-prone site of Aβ and is often termed the self-recognition site [28-30]. Many rationally designed peptides retain the LVFFA sequence, with the hope that the inhibitor peptide will selectively bind to the analogous sequence of natural Aβ42 [28, 31-34]. What often differs among these peptides are the N and C–terminal amino acids surrounding the LVFFA core. These surrounding residues are thought to act as aggregation blockers (termed β-sheet breakers), preventing additional amyloid peptides from adhering to the Aβ-peptide complex [35]. Many of these LVFFA peptides, and their later-generation variants, have been shown to inhibit Aβ aggregation at stoichiometric concentrations and rescue living cells from the toxic effects of Aβ42. For example, Ganno and coworkers recently synthesized and studied 15 different variants having KLVFF as the core sequence (additional residues were added to the N-terminus and/or the C-terminus of this core sequence) [31]. From Thioflavin T and transmission electron microscopy experiments, nearly all of these peptides possessed some ability to inhibit aggregation at a 1:1 molar ratio (40 μM peptide to 40 μM Aβ40). Several peptides inhibited aggregation by approximately 80% compared to samples lacking the inhibitory peptides. Atomic force microscopy was used to identify the aggregation products of Aβ40 alone, the peptides alone and Aβ40 in the presence of the peptide inhibitors. Several peptides were found to self-aggregate into spherical assemblies, yet still showed inhibitory capacity. They found that placing positively charged residues at the N-terminal end of the KLVFF sequence were less likely to inhibit than if positive amino acids were placed at the C-terminal end. The authors also concluded that the peptides with the highest affinity to Aβ40 showed the greatest ability to inhibit amyloid-based aggregation. These results seem to be typical of the KLVFF core peptide inhibitors. These peptides demonstrate the potential of rationally designed peptide inhibitors as amyloid blocking agents.

### Table 1. Peptide Inhibitors of Aβ42

<table>
<thead>
<tr>
<th>Aβ42 Mimics</th>
<th>KLVF</th>
<th>Ref</th>
<th>[28]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[31]</td>
</tr>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[34]</td>
</tr>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[60]</td>
</tr>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[38]</td>
</tr>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[60]</td>
</tr>
<tr>
<td></td>
<td>KLVF</td>
<td>KLVF</td>
<td>[60]</td>
</tr>
</tbody>
</table>

### Table 2. Peptide Inhibitors of IAPP

<table>
<thead>
<tr>
<th>IAPP Rodent</th>
<th>S NVGSNTY</th>
<th>Ref</th>
<th>[65]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R--L--P--V--F--P</td>
<td>[70]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R--L--P--V--F--P</td>
<td>[70]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S NNF GA</td>
<td>[73]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GAIL SST</td>
<td>[73]</td>
<td></td>
</tr>
</tbody>
</table>
The hydrophobic core of Aβ42 is not the only region targeted for inhibition of aggregation. Aβ42 aggregation has been inhibited using C-terminal fragment (CTF) sequences of various lengths [36-38]. The best of these inhibitors spanned the final 13, 11 and 4 amino acids of Aβ42 [38], indicating that the length of the inhibitor peptide did not necessarily correlate with inhibitory propensity. Instead, the best correlation between CTF and their physical properties appeared to rely on the ability of the CTF to form a coil-turn conformation [38]. This conformation seems to appear in other inhibitory models, such as the peptide hairpin inhibitor of Teplow and coworkers [39]. While this peptide does contain one D-amino acid (D-Proline), the polypeptide is believed to form a hairpin turn held together by a disulfide bridge.

The rationally designed peptides have proven to be a strong class of inhibitory agents for Aβ42. These peptides continue to be modified with the ultimate goal to increase their ability to inhibit amyloid aggregation. Many of these peptides have been found to protect living cells from toxic amyloid aggregates. Perhaps future iterations of these peptides will show even greater ability to protect cellular viability.

**Peptide Inhibitors of Aβ Aggregation Selected from Combinatorial Libraries**

Advances in molecular biology, coupled with the decreased cost of DNA synthesis, have led to a greater ability to generate high-quality gene/protein libraries [40]. Libraries that once took months to construct, can now be done in a matter of weeks. While the ability to construct gene libraries has greatly evolved over the past decade, the ability to select for those variants that show a desirable activity has not. There are very few techniques in the literature that describe screens to select for peptides that inhibit amyloid aggregation and protect living cells from toxic protein aggregates. Despite this paucity of screening techniques, those screens that have been utilized have proven to be successful at identifying multiple amyloid-inhibiting peptides. We will discuss each of these screening techniques and the inhibitory peptides they have identified.

**Peptides Identified Using Phage-Display**

Phage display has proven to be an excellent method for screening large libraries of peptides to select for those that bind to an epitope of interest [41]. Many of the libraries screened by phage display have targeted large peptides/proteins. These libraries of larger peptides have generated sequences that inhibit Aβ aggregation, but may prove difficult to convert into a therapeutically useful drug. For example, several papers have been published recently that describe antibody-based, affibody, and other scaffold-based proteins selected by phage display [42-52]. Many of these selected proteins have been shown to inhibit aggregation, but their therapeutic potential remains untested.

Kamijo and coworkers recently screened a randomized heptapeptide library against Aβ42 [53]. Their goal was to identify peptides that could bind Aβ42, but did not necessarily possess sequence similarities to Aβ42. They identified several peptides, rich in arginines, that showed in vitro ability to inhibit Aβ42 aggregation. Size-exclusion chromatography and SDS-PAGE gel-shift assays indicated that several of these selected peptides kept Aβ42 from forming soluble oligomers [53]. Additional experiments will need to be performed to assess how these peptides inhibit aggregation. Of specific interest is why arginine-rich sequences were highly selected in this screen.

Not all peptides identified with phage display have been found to inhibit aggregation. Kiessling and coworkers identified several peptides that could bind to different aggregation states of Aβ40 [54]. While several peptides were identified that could bind to Aβ40, none slowed the rate of aggregation, and many increased aggregation. Therapeutically, this increase in aggregation could be beneficial if, in fact, aggre-

---

**Fig. (1).** (A) Amyloidogenic peptides, such as Aβ42 and IAPP self-assemble, ultimately leading to the formation of amyloid. (B) When linked to an amyloid peptide, EGFP does not fold or fluoresce. The aggregation of the amyloid peptides prevents proper folding and fluorescence of EGFP. (C) Inhibitors that prevent the self-assembly of the amyloid peptides allow the EGFP to fold and fluoresce.
showed the greatest fluorescence. Using this screen, we identified two hydrophobic regions of Aβ42. Both peptide libraries were designed to mimic the hydrophobic patches of Aβ42 proteins to an Aβ42 library peptide complex. The library peptides that prevent the aggregation of additional Aβ42 proteins to an Aβ42-library peptide complex. The library peptides are designed to act as two-sided patches; one

gated Aβ is less toxic than small oligomers. These aggregation-enhancing peptides may function to help sequester Aβ40 into less toxic fibrils rather than the more toxic soluble oligomers.

Peptides Identified Using Aβ42-EGFP

Hecht and coworkers described the use of a GFP-based screen to assess the in vivo aggregation propensity of Aβ42 in E. coli cells [29, 55]. This screen has been used to assess the aggregation potential of Aβ mutants [55-57] as well as to screen for small molecules that can inhibit aggregation [58]. We recently used this screen, replacing GFP with enhanced GFP (EGFP) to select for mutants of IAPP that resisted aggregation [59]. In this screen, the amyloid protein (such as Aβ42 or IAPP) is genetically fused to the reporter protein EGFP. When expressed in E. coli, the Amyloid-EGFP fusion proteins produce virtually no green color or fluorescence due to the propensity of the amyloid proteins to aggregate (Fig. 1). However, when the amyloid proteins are prevented from aggregating (either by mutagenesis or in the presence of an aggregation inhibitor), the fused EGFP folds and fluoresces brightly.

We have recently used this screen to select peptides from different combinatorially randomized libraries for their ability to inhibit Aβ42 aggregation [60]. Combinatorially diverse library peptides were co-expressed in E. coli with the Aβ42-EGFP fusion protein. Peptides that prevented the aggregation of the Aβ42 allowed EGFP to fold and fluoresce. Individual E. coli colonies expressing both a library peptide and amyloid-EGFP were screened to select for those colonies that showed the greatest fluorescence. Using this screen, we identified three short peptides capable of inhibiting Aβ42 aggregation [60]. We believe this screen can be used to select for increasingly potent inhibitors of Aβ42 by improving the selection conditions and the combinatorial library design.

Gene libraries can be easily constructed using a variety of techniques. Gene libraries can be designed to encode for short peptides targeted to anneal to, and disrupt aggregation of, the amyloidogenic Aβ42 peptide. For example, Fig (2) shows two peptide libraries targeted to mimic each of the two hydrophobic regions of Aβ42. Both gene libraries were constructed using synthetic single-stranded oligos [61] and pieced together using oligo overlap and extension (Fig. 3). Gene variability was introduced to the gene libraries by using degenerate codons encoding for combinatorial mixtures of amino acids (Table 3).

Both peptide libraries were designed to mimic the hydrophobic patches of Aβ42, with the intention of producing peptides that could anneal to the monomeric form of Aβ42. Also designed into the peptide libraries are strongly polar and charged aspartic acid residues. These acidic residues are intended to incorporate a strongly charged “bump” on the library peptides that prevents the aggregation of additional Aβ42 proteins to an Aβ42-library peptide complex. The library peptides are designed to act as two-sided patches; one

Table 3. Oligos Used for the Construction of Gene Libraries 1 and 2

| Library 1 Forward | 5'-CTAGCTGT CAT ATG TCT AAC AAA GGC GCG ANT ANT GNT CTG ATG GNT GNT GNT GNT ATT GCG GAT AGT CAT AGT TAA-3' |
| Library 2 Forward | 5'-CTAGCTGT CAT ATG CAG AAA CTG GNT DTA DTA GCG GAA GNT GNT GGC TCT AAC AAA TAA ATT GCG GAT AGT CAT AGT TAA-3' |
| Reverse | 5'- GATAGGAC GAATTC CAT ATG TCT AAC AAA GGC GCG ANT ANT GNT CTG ATG GNT GNT GNT GNT ATT GCG GAT AGT CAT AGT TAA-3' |

Degenerate codons are underlined. Complementary regions are colored blue. All oligos are written from 5'-3'. N: equal mixture of A, T, G and C. D: Equal mixture of A, G and T.

| Aβ42: DAEFRHDSGYEVHHQKLVVFAEDVGSNKGAIIGLMVGGV Via | MSNKGIVLMMVVVI AdSHS |
| Library 1: TTA AAAA NND DDDDD SSM GGGG |
| Library 2: ALL AA DII DD GMM GG VV |

Fig. (2). Amino Acid Sequences of Aβ42 and Library 1 and Library 2 Peptides. The amino acid sequence for Aβ42 is shown. Library 1 was constructed to have mixtures of amino acids in the bold-faced positions. Degenerate gene construction: Codon ANT encodes for an equal mixture of I, T, N and S. Codon GNT encodes for an equal mixture of V, A, D and G. Codon NTN encodes for a mixture of F, L, I, M and V.

Table 3. Oligos Used for the Construction of Gene Libraries 1 and 2

| Library 1 Forward | 5'-CTAGCTGT CAT ATG TCT AAC AAA GGC GCG ANT ANT GNT CTG ATG GNT GNT GNT GNT ATT GCG GAT AGT CAT AGT TAA-3' |
| Library 2 Forward | 5'-CTAGCTGT CAT ATG CAG AAA CTG GNT DTA DTA GCG GAA GNT GNT GGC TCT AAC AAA TAA ATT GCG GAT AGT CAT AGT TAA-3' |
| Reverse | 5'- GATAGGAC GAATTC CAT ATG TCT AAC AAA GGC GCG ANT ANT GNT CTG ATG GNT GNT GNT GNT ATT GCG GAT AGT CAT AGT TAA-3' |

Degenerate codons are underlined. Complementary regions are colored blue. All oligos are written from 5'-3'. N: equal mixture of A, T, G and C. D: Equal mixture of A, G and T.

| Aβ42: DAEFRHDSGYEVHHQKLVVFAEDVGSNKGAIIGLMVGGV Via | MSNKGIVLMMVVVI AdSHS |
| Library 1: TTA AAAA NND DDDDD SSM GGGG |
| Library 2: ALL AA DII DD GMM GG VV |

| Aβ42: DAEFRHDSGYEVHHQKLVVFAEDVGSNKGAIIGLMVGGV Via | MSNKGIVLMMVVVI AdSHS |
| Library 1: TTA AAAA NND DDDDD SSM GGGG |
| Library 2: ALL AA DII DD GMM GG VV |

| Aβ42: DAEFRHDSGYEVHHQKLVVFAEDVGSNKGAIIGLMVGGV Via | MSNKGIVLMMVVVI AdSHS |
| Library 1: TTA AAAA NND DDDDD SSM GGGG |
| Library 2: ALL AA DII DD GMM GG VV |

| Aβ42: DAEFRHDSGYEVHHQKLVVFAEDVGSNKGAIIGLMVGGV Via | MSNKGIVLMMVVVI AdSHS |
| Library 1: TTA AAAA NND DDDDD SSM GGGG |
| Library 2: ALL AA DII DD GMM GG VV |
side being sticky and annealing to monomeric Aβ42, and the other side presenting a repulsive residue (or residues) that prevent additional Aβ42 peptides from annealing.

The gene library is cloned into one plasmid and cotransformed with the amyloid-EGFP plasmid into a suitable _E. coli_ expression host (Fig. 4). The resultant colonies are transferred to plates that can induce protein expression. With this system, thousands of transformed colonies can be screened to identify those few that show elevated levels of EGFP fluorescence.

**PEPTIDE INHIBITORS OF IAPP AGGREGATION**

In type II diabetes the amyloid-forming peptide is islet amyloid polypeptide (IAPP, amylin). This 37 amino acid polypeptide misfolds and forms toxic aggregates within the pancreas. This misfolding into toxic aggregates, such as small soluble oligomers or large fibers, is believed to contribute to the loss of pancreatic β-cells. A great debate continues within the scientific community to identify the toxic form (or forms) of IAPP. While the exact role of IAPP in type II diabetes is unclear, it is known that IAPP is found as extracellular deposits of amyloid in approximately 90% of patients afflicted with type II diabetes [61-63]. This peptide is highly amyloidogenic, finding any substance to inhibit its aggregation could be a potent weapon in the fight against type 2 diabetes.

It is well established that rodent IAPP (rIAPP) is nonamyloidogenic and nontoxic. It is also established that rats and mice are not known to develop type II diabetes [64], strengthening the argument that inhibiting IAPP aggregation could help to prevent type 2 diabetes. Rodent IAPP, which differs from human IAPP by six amino acids, has been demonstrated to be capable of inhibiting human IAPP aggregation [65].

Five of the substitutions known to convert amyloidogenic human IAPP into non-amyloidogenic rodent IAPP occur in the 20-29 region of the peptide (Table 2). Because of these substitutions the 20-29 region has long been described as the amyloidogenic region of IAPP [32, 66, 67]. Recent studies have indicated that several mutations outside of the 20-29 region can hinder fibrillogenesis, and are likely important for aggregation [59, 68-74]. Several short peptides targeting this aggregation-prone region have been identified [73]. Additionally, a single mutation in the middle of this aggregation region, I26P, has been shown to act as a potent inhibitor of IAPP aggregation [70].

**Fig. (3).** Oligo overlap and extension: Single-stranded DNA oligos were designed having complementary 3' overhang regions (dashed lines). When mixed, the complementary regions anneal and act as templates for Klenow Fragment catalyzed DNA synthesis. Nucleotides not involved in annealing (solid lines) can be explicitly designed base by base or combinatorially varied.

**Fig. (4).** Construction and selection of peptide libraries. Cotransformed cells were plated on nitrocellulose absorbed on LB plates containing Ampicillin and Streptomycin. After incubation, resulting colonies are transferred to LB plates containing IPTG. Green-colored colonies are selected and analyzed.
Insulin is an additional peptide that is known to inhibit IAPP aggregation [75]. Insulin is co-secreted with IAPP from pancreatic B-cells. While the exact role these two peptides play in the development of type 2 diabetes remains to be determined, it is not surprising that this metabolism-driving hormone is important in preventing IAPP aggregation. Raleigh and coworkers were able to determine the crystal structure of IAPP fused to maltose binding protein [76]. Based on the structure of IAPP in this fusion protein, they were able to model the possible binding interaction between IAPP and the B-chain of insulin, showing the importance of IAPP Phe15 in this aggregation (Table 2 shows the sequence of insulin as well as the residues of insulin suggested as interacting with IAPP).

In one of the few articles describing short peptide inhibitors of IAPP aggregation, Fraser and coworkers tested a series of hexapeptides, each overlapping with a segment of IAPP [73]. When co-incubated with IAPP, several of the peptides, such as GALILST appeared to decrease the density of fiber formation. More importantly, one peptide SNNFGA (Table 2) had the ability to rescue cultured cells from IAPP toxicity.

OUTLOOK

Over the past decade, we have witnessed a great increase in the number of articles describing short peptides as inhibitors of amyloid aggregation. Advances in molecular biology (which allows for the inexpensive synthesis of DNA libraries) and peptide synthesis (which have lowered the costs of chemically synthesizing peptides) have made it possible to both identify and synthesize specific peptides capable of inhibiting aggregation. While it remains to be seen whether short peptides can be used as therapeutic agents in preventing the amyloid diseases, these short peptide inhibitors can aid in identifying the aggregation-prone regions of the amyloid proteins. These short peptide inhibitors can also be useful in identifying the important characteristics of potential therapeutic agents in amyloid inhibition. Perhaps future iterations of peptides will be identified that can protect cells from amyloid aggregates as well as resist our body’s natural protein degradation machinery.

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENTS

We thank Luiza A. Nogaj for critical reading of this manuscript. Funding for this work was from the National Institutes of Health (1R15AG032582).

ABBREVIATIONS

IAPP = Islet amyloid polypeptide
Aβ = Amyloid β-protein
EGFP = Enhanced green fluorescent protein.

REFERENCES


Short Peptides as Inhibitors of Amyloid Aggregation

The Open Biotechnology Journal, 2011, Volume 5


[48] Smith TJ, Stains CI, Meyer SC, Ghosh I. Inhibition of beta-amyloid fibrilization by directed evolution of a beta-sheet presenting minia-


[69] Abedini A, Meng FL, Raleigh DP. A single-point mutation converts the highly amyloidogenic human islet amyloid polypeptide


