Amylin Amyloidosis

- Amylin is a 37 aa peptide that is co-secreted with insulin by β cells.
- Amylin amyloid formation occurs in type 2 diabetes, with amyloid fibril deposits being present in the islets of Langerhans.
- Amylin amyloid plaques are present in at least one islet of 90% of subjects with type 2 diabetes.
- Extensively amylin amyloid is correlated with islet dysfunction in animal models and with the requirement for insulin replacement therapy in humans.

6. Functional Amyloid

Not All Amyloids Are Bad

- Amyloid can be a functional protein fold that does not cause pathology in the organism that produces the amyloid.
- Functional amyloids have been identified in fungi, where fungal prions (Sup35 and Het-S) act as non-genetic inheritable elements.
- *E. coli* and salmonella produce functional amyloids: curli fibres.
- Humans also produce functional amyloids in granules of melanocytes and hormone producing cells.

Pmel17 and Melanosomes

- Melanosomes are pigment granules produced by melanocytes and retinal pigment epithelium.
- Melanin is a pigment produced in these granules, and is a tyrosine based polymer.
- Pmel17 is a protein present in pigment granules and mutations in this protein in mice result in the loss of pigmentation.
- Pmel17 forms amyloid fibrils in the melanosomes onto which melanin is deposited.

Peptide Hormones are stored as Amyloid Fibrils in Pituitary Secretory Granules

- The pituitary is an important endocrine gland that produces a number of important peptide hormones that are stored in granules.
- Prolactin, ACTH, β-endorphin, oxytocin are stored in these granules as amyloid fibrils.
- Upon secretion, the fibrils dissociate due to an increased in pH into monomers.
- In addition, other peptide hormones such as glucagon (pancreas) and calcitonin (thyroid) can form amyloid suggesting that peptide hormones could be stored in different secretory cells as amyloid.