Amylin Amyloidosis

- Amylin is a 37 aa peptide that its 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