

Robotic selection of RNA aptamers against amyloid proteins and peptides.

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RNA aptamers have been shown to bind with affinity and specificity akin to antibodies. Aptamers have a number of advantages over antibodies including that they can be raised rapidly against any target and are non-immunogenic. Based upon the methods of Cox & Ellington, we have been able to automate the selection of such aptamers utilising a Biomek 2000 liquid-handling robot (Beckman Coulter).

Over 20 human proteins have been shown to form amyloid fibrils leading to many different pathologies. These range from the A β peptide in Alzheimer's disease, where fibrils of A β appear to be the proximate cause of neurodegeneration, to β -2-microglobulin which can form fibrils in haemodialysis related amyloidosis. Current strategies for preventing or controlling amyloid pathologies are directed against blocking self-association of precursor proteins/peptides or clearing/destroying the fibrils that form. The latter approach includes the use of immunisation to "vaccinate" against the fibrils, e.g. in Alzheimer's disease, although neither approach has yet been successful and each has its own technical problems to overcome.

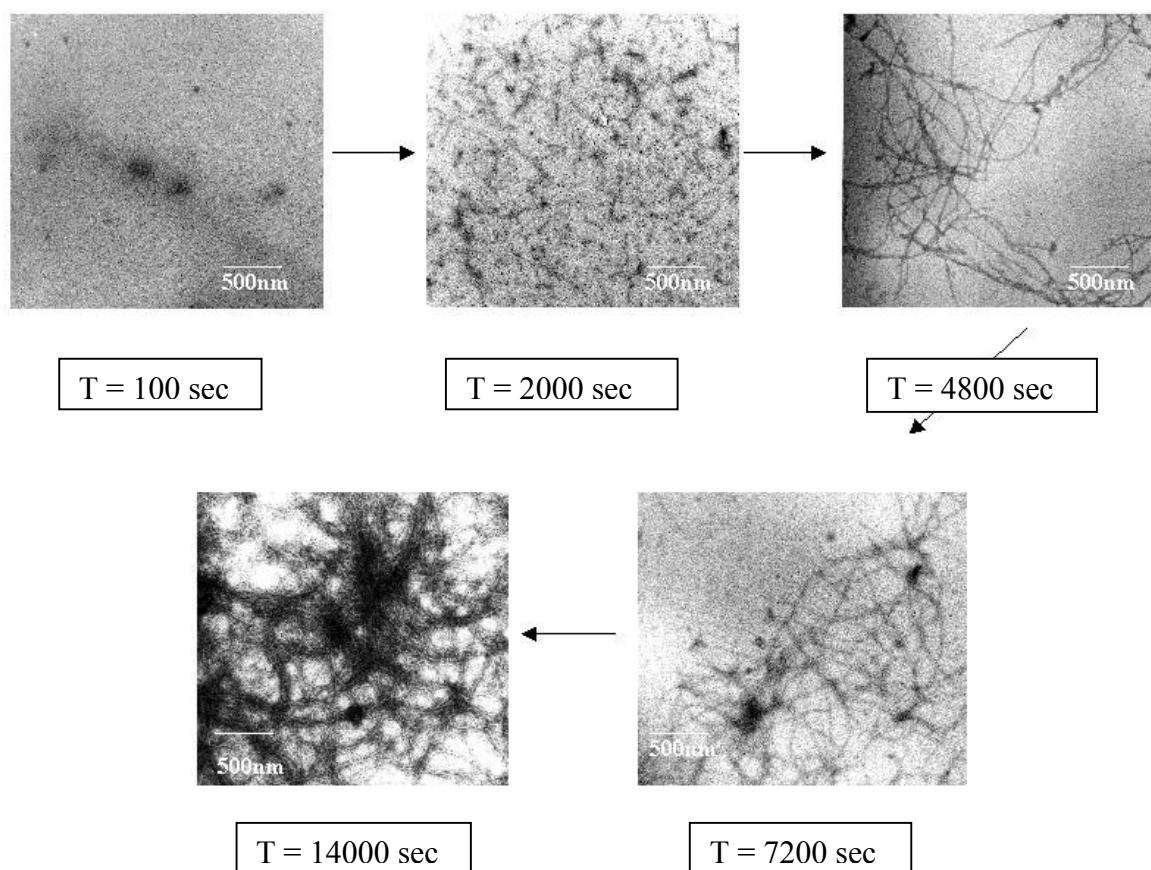


Fig. 1: Electron microscopy time course of amyloid fibril formation by A β peptide.

Aptamers have been selected against A β fibrils, protofibrils & oligomers (see Figures 1 & 2) as well as mature and immature β ₂M fibrils and native β ₂m. The initial aptamer isolates have affinities in the micromolar range. Anti-A β aptamers have been isolated for the D-amino acid enantiomer of the peptide allowing reflection of the resultant aptamer sequences into

aptamers based on L-ribose. The latter are stable in biological environments. These aptamers could potentially be used as diagnostic or therapeutic agents.

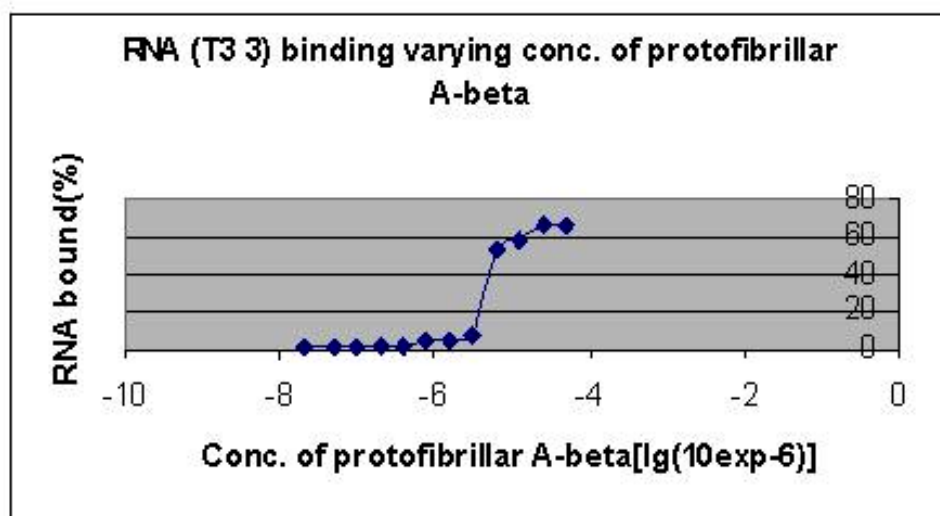


Fig. 2: Filter-binding assay of one of the aptamers selected against proto-fibrils shown in Fig. 1..

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