Amyloidosis: Structure of a λ 6 Light Chain Antibody Fragment

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It has been well evidenced the preferential association of the lambda VI antibody light chain subgroup with antibody light chain amyloidosis. We have generated an engineered light chain variable region domain (rVL6aJL2) whose 99 amino terminal residues are encoded by the germline VI gene segment 6a and the complementary segment of 12 residues encoded by the gene segment JL2. *In vitro* fibril formation assays demonstrated that the rVL6aJL2 is able to slowly aggregate itself as amyloid-like fibrils under physiological conditions. The recombinant protein expressed in *E.coli*, was purified and crystallised using 1.4 to 2.0 M sodium acetate, 100mM MES pH 6.5. Crystals diffracted up to 1.9 Å resolution. The crystals grew in three different space groups and all contained fibrilar structures assembled into the crystal. These structures have helicoidal shape with a 93 Å long pitch, and a section perpendicular to the axis, 45 Å wide, with a squared shape. The molecule that generates this structure through a 4_1 symmetry, is a dimer built as that formed by light and heavy chains in functional antibodies. These dimer-dimer contacts found, comprises a surface larger than 1600 $Å^2$ and the amino acids involved has been shown to participate in fibrillogenesis. As in other structures from fibrillogenic antibody light-chains, no significant conformational changes have been observed. The question we have so far is: have or not the helicoidal structures we found over 3 different space groups relation with the atomic structure of amyloidotic fibers?

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