In silico intrinsic disorder analysis of β-crystallin B2 protein and mutations that cause congenital cataract

J. B. O. Souza, J. E. A. Júnior, E. R. Tomarozzi and S. Giuliatti

FMRP/USP

The congenital cataract is one of the major causes of visual deprivation in the world affecting 3 in every 10,000 live newborns in developing countries. Approximately 50% of children's cataracts are due to the genetic cause and the majority of autosomal dominant. The condition may be identified mainly based on the opacity in the ocular lens, and it is the result of some specific proteins loss of function. Singular mutations in the beta-crystalline B2 protein (CRYBB2) are one of the major causes of congenital cataract that affects several members of the same family, emphasizing the importance of this protein in the physiopathology of the disease. The CRYBB2 has regions of intrinsic disorder (ID) that can be indispensable in their role. ID regions show high number of interaction sites which are associated with cell signaling, becoming the target so that the unwanted interactions can be avoided. Thus, changes in the particular pattern of the ID proteins can cause cellular malfunction, favoring the occurrence of diseases. The aim of this study was to predict and analyze through in silico tools, the CRYBB2 protein intrinsic disorder (ID) and A2V, I21N, S31W, W59C, D128V, V146M, W151C, V187M and R188H mutant proteins, that cause congenital cataracts, in order to check for changes in the ID pattern caused by singular mutations in the protein. The ID's prediction was performed by ANCHOR and IUPred computational tools. The ANCHOR tool showed three ID regions. The first region is in interval of 15-25 aminoacids, where the I21N mutation occur that causes ID decrease in the mutated protein. The second one is in interval of 52-60, where the W59C mutation happen that caused ID increase. The third region is in interval of 151-16 where the W151C mutation is located which also causes increased ID. The IUPred tool also showed 3 ID regions. The first one in interval of aminoacids 1- 42, where the A2V, I21N and S3I mutations happen which cause ID decrease in this region. The second region is in interval of 94-99, however, to date, there are no known mutations in this range. The third region is in interval of 175-190, where the V187M and R188H mutations occur, where the V187M mutation causes an ID increase and R188H mutation did not change in the ID wild CRYBB2 protein pattern. Therefore, it is concluded that missense mutations were enough to promote alterations in the CRYBB2 mutated protein intrinsic disorder pattern.