**DAY 5 HOMOLOGY MODELLING**

**AIM:**

To discover a drug for the inhibition of the enzyme acetylcholinesterase to prevent the action of beta amyloid protein on the brain cells

**PRINCIPLE:**

Treatment of Alzheimer's disease has been dominated by the use of acetylcholinesterase (AChE) inhibitors. These drugs compensate for the death of cholinergic neurons and offer symptomatic relief by inhibiting acetylcholine (ACh) turnover and restoring synaptic levels of this neurotransmitter. Recently, however, AChE itself has been implicated in the pathogenesis of Alzheimer's disease. In particular, it appears that AChE may directly interact with amyloid-beta in a manner that increases the deposition of this peptide into insoluble plaques. This new role suggests that properly designed AChE inhibitors might be able to act as disease-modifying agents rather than as mere palliatives. Additionally, numerous studies have suggested that cholinergic modulation and other functional consequences of AChE inhibition may affect amyloid precursor protein processing and protect neurons against a variety of insults. It therefore seems likely that new AChE inhibitors, which capitalize on all these strengths would be excellent candidates for future Alzheimer's disease therapy.

**Sequence of the protein from uniprot**

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK

TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG

EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR

GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE

EADDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC

RAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAMSQSLLKTTQEPLARD

PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA

KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITAL

QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER

MNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISYGNDALMPSLTET

KTTVELLPVNGEFSLDDLQPWHSFGADSVPANTENEVEPVDARPAADRGLTTRPGSGLTN

IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL

VMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN





