

Structural information on Receptor Proteins leads to new possible cancer therapies



NanoBio Project

4th semester

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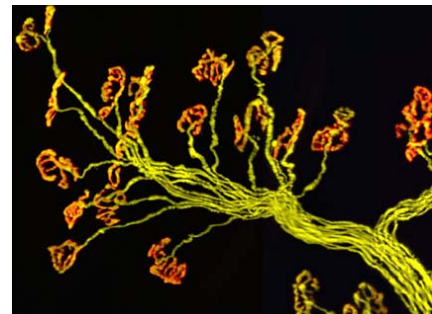
www.nanobio.dk

Project description at:

<http://www.nanobio.dk/sempages.asp?mid=54&sid=2004>

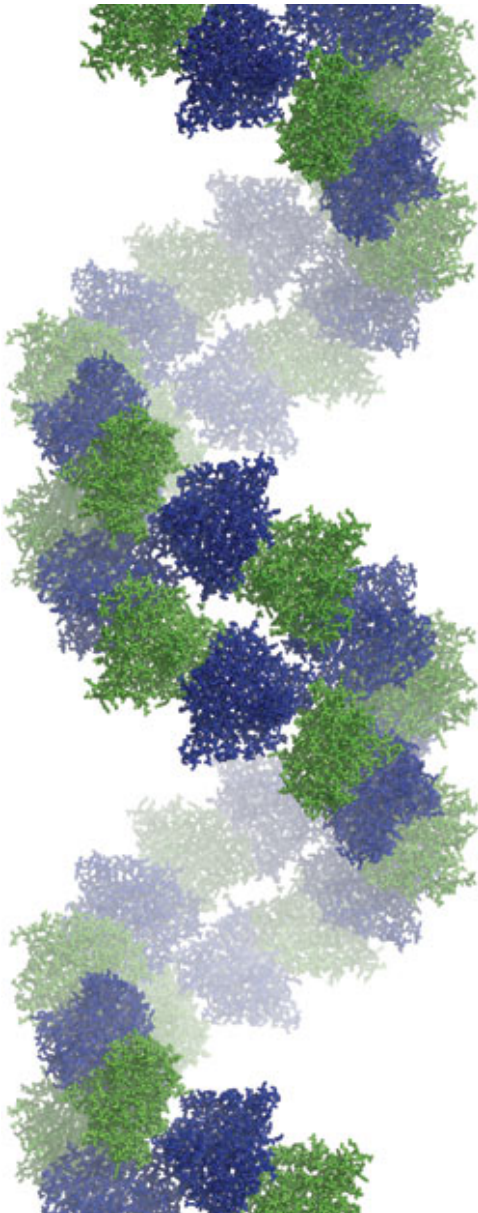
The 3D structure of a protein has an obvious beauty to it – yet it represents an incredible complexity. The 20 amino acids are coupled to one another – thus for a 100 Amino Acid Protein, there is a staggering 20^{100} different ways one can construct a sequence of such a protein. The conformational space that in principle is accessible to the protein given that the sequence is known is of almost cosmic proportions. Yet proteins in nature typically fold perfectly and rapidly (within a few milliseconds). It is still mostly a mystery how nature accomplishes this feat – despite the fact that our lives depend on exactly this fantastic feature. Understandably many science groups have been working on this topic – but many in vain. The analyses of the proteins' primary, secondary and tertiary structure gives a vast amount of information about the proteins function and even how to modulate protein function.

Growth factors and their trans-membrane receptor tyrosine kinases play important roles in cell proliferation, survival, migration and differentiation. One group of growth factors, comprising epidermal growth factor (EGF)-like proteins and neuregulins, stimulates cells to divide by activating members of the EGF receptor (EGFR) family, which consists of the EGFR itself and the receptors known as HER2–4. This highly conserved signaling module plays a fundamental role in the morphogenesis of a diverse spectrum of organisms, ranging from humans to nematodes, and has also been implicated in the development and growth of many types of human tumour cells. In humans, more than 30 ligands and the EGFR family of four receptors lie at the head of a complex, multi-layered signal-transduction network.



Some earlier bioinformatics work done by the Nanobio group has revealed that membrane receptors like EGFR (Epidermal Growth Factor Receptor) contained exactly the motifs that makes proteins highly sensitive to UV light and lead to the prediction that UV light could modify these receptors permanently and stop

cancer proliferation. Since the EGF receptor is often over-expressed in cancers and other proliferative skin disorders, it might be possible to significantly reduce the proliferative potential of these cells upon UV illumination. A combination of bioinformatics, biophysical, advanced laser studies and cell biology lead to the realization that laser-pulsed UV light stops cancer growth and induces apoptosis. We have previously shown that laser-pulsed UV (LP-UV) illumination of two different skin-derived cancer cell lines both over expressing the EGF receptor, lead to arrest of the EGFR signaling pathway.



Data Bases and Programming

Much of the database exists as a large number of excel files – so you need to be able to read and use excel files, and be willing to learn how to merge information from several excel files. A highly useful tool for the project is MATLAB – and we will develop all visualization of the data (1D, 2D or 3D) in MATLAB, which is excellent for this use. We will also learn how to create Graphical User Interfaces in MATLAB. These skills the project team is likely to benefit from in many future activities as well.

Project Target

This project will focus on creating tools to investigate proteins 3D structures as documented in the Protein Data Bank files that are publically available. We will identify structural motifs that statistically appear to be of interest, and develop tools based on MATLAB to visualize and analyze the structure of the proteins.

Potentials:

If we succeed in finding new packing information, or explaining the observed one, it is likely that we will be able to publish it. In case this happens, the project team will co-author the manuscript.