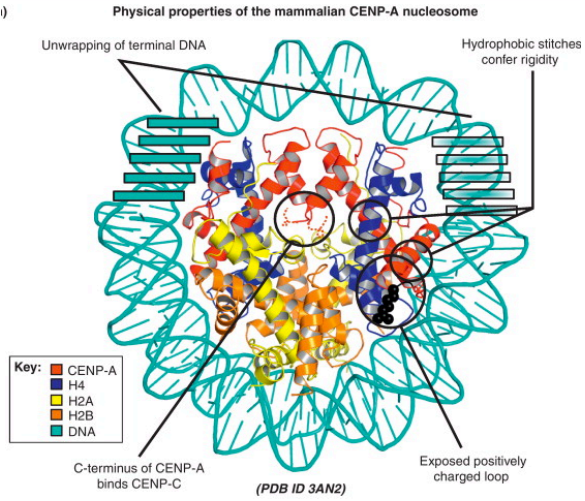
MASTER Project: NUCLEOSOME BIOLOGY

A Master thesis project is available at The University of Oslo, based in the Sekulic lab at NCMM (Centre for Molecular Medicine Norway).

The aim of the project is to understand chromatin organization of the centromeres at molecular level. The centromere is a part of the chromosome that serves as the foundation for the formation of kinetochore, the protein structure that attaches duplicated chromosomes to opposite poles of the dividing cell. The student will gain hands-on experience in the purification of DNA, histones and other centromeric proteins using state-of-the-art technologies. He/she will assemble nucleosomes and nucleosome arrays *in vitro* for further biophysical analysis.

Understanding how DNA is packed in our cells, and how chromatin conformation is used as a basis for specifying the centromere is essential. Without a functional centromere, chromosomes are lost or broken – a hallmark of cancers. The project is expected to last for 6 – 12 months. If you are interested please contact Nikolina Sekulic (Nikolina.sekulic@ncmm.uio.no)



Sekulic and Black, Trends Biochem Sci, 2012

Literature:

1. **Sekulic N**, Black BE. Preparation of Recombinant Centromeric Nucleosomes and Formation of Complexes with Nonhistone Centromere Proteins. ***Met Enzymol***. 2016;573:67-96. doi: 10.1016/bs.mie.2016.01.014.

2. Falk JS*, Guo JY*, **Sekulic N***, Smoak EM*, Mani T, Logsdon G, Gupta K, Jansen LT, Van Duyne GV, Vinogradov SA, Lampson MA, and Black BE. CENP-C reshapes and stabilizes CENP-A nucleosomes at the centromere. ***Science.*** 2015 May 8;348(6235):699-703
* - Denotes equal contributions - co-authorship

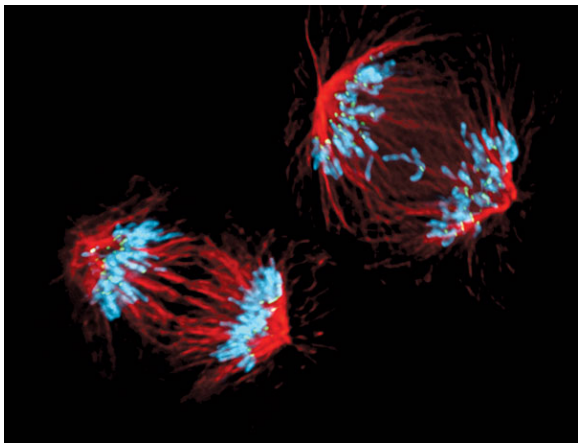
3. **Sekulic N**, Bassett EA, Rogers DJ, Black BE. The structure of $(CENP\text{-}A\text{-}H4)_2$ reveals physical features that mark centromeres. ***Nature***. 2010 Sep 16;467(7313):347-51

MASTER Project: MOLECULAR BASIS OF GENOME STABILITY

A master thesis project is available at The University of Oslo, based in the Sekulic lab at NCMM (Centre for Molecular Medicine Norway).

The aim of the project is to use biochemical and biophysical techniques to characterize molecular interactions at the centromere, which are assuring equal segregation of chromosomes during cell division. The student will gain hands-on experience in molecular cloning, bacterial expression and the purification of proteins, using state-of-the-art equipment.

Final stages of the project include assembly of multi-protein complexes, protein crystallization and the use of X-ray crystallography to obtain 3D structures of the complex. The knowledge gained in this project will provide insight into the major mechanisms that safeguard our genome during chromosome segregation, and will



The left cell is dividing properly, but the right one shows a chromosome segregation defect. The chromosomes are blue and the microtubules are red.

help build a better understanding of how this safety mechanism is broken in cancer. The project is expected to last for 6 – 12 months. If you are interested please contact Nikolina Sekulic (Nikolina.sekulic@ncmm.uio.no)

Literature:

Watanabe, Y. Shugoshin: guardian spirit at the centromere. Curr. Opin. Cell Biol. 17, 590–595 (2005).

MASTER Project: COMPUTATIONAL PROTEIN MODELLING

A master thesis project is available at The University of Oslo. The project is a collaboration between the Sekulic lab at NCMM (Centre for Molecular Medicine Norway) and the Cascella group at The Department of Chemistry, UiO (https://www.mn.uio.no/kjemi/english/people/aca/michelec/). The project combines biology, chemistry, physics and computational techniques. The major goal is the computational modelling of an enzyme, Aurora B, that is a cancer drug target.

The student is expected to explore molecular dynamics of the enzyme (protein kinase) in phosphorylated (active) and unphosphorylated (inactive) form. We use hydrogen-deuterium exchange to experimentally measure dynamic differences between the two different forms of the enzyme. The knowledge gained from computational modelling, together with the collected experimental data will contribute to a better understanding of the process of enzyme activation, and it will serve as a basis for the generation of new, more potent

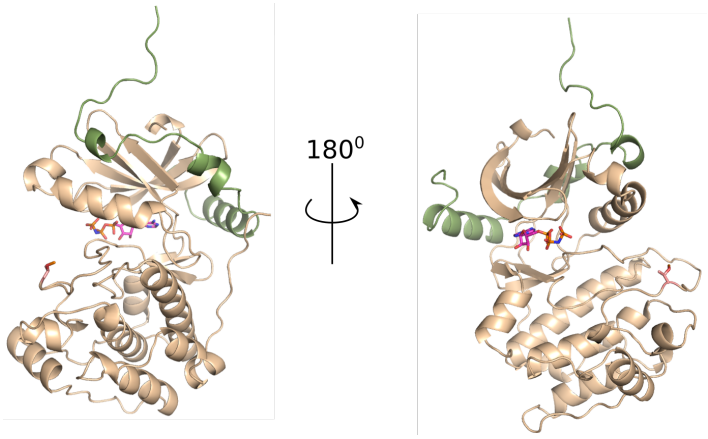


Photo credit: Dario Segura

Understanding the role of flexibility in the enzyme activity might be exploited in engineering effective drugs for specific cancer targeted therapy.

cancer therapies.

The project is expected to last for 6 – 12 months. If you are interested please contact Nikolina Sekulic (Nikolina.sekulic@ncmm.uio.no).

Literature:

1. Zaytsev AV[1], Segura-Peña D[2], Godzi M[1,3], Calderon A[2], Ballister ER[2], Stamatov R[1], Mayo AM[2], Peterson L[4,5], Black BE[6], Ataullakhanov FI[3,7,8], Lampson MA[2], Grishchuk EL[1]. Bistability of a coupled Aurora B kinase-phosphatase system in cell division. Elife. 2016 Jan 14;5:e10644. doi: 10.7554/eLife.10644.