***EnveloProg*: Nuclear Envel**ope Architecture in Prostate Cancer **Prog**ression

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One of the criteria that pathologists use for diagnosis of cancer include many morphologically distinctive alterations in the nucleus, a cell's largest organelle. Nuclei of tumor cells typically show abnormal shape and size, often exhibiting altered structure of **the nuclear envelope that separates the nucleus from the cytoplasm**. Some components of the nuclear envelope have been previously shown to be altered in prostate tumors and their destabilization was shown to promote metastasis. However, the architecture of nuclear envelope has never been investigated in a detailed and quantitative manner in prostate cancer.

Prostate cancer is among the most frequent cancer in men. The five-year survival of localized prostate cancer is estimated as nearly 100%, whereas in cases of metastatic disease is only 29%. Therefore, there is a need to understand the process of prostate cancer progression and dissemination including the potential components involved. In the proposed project, I hypothesize **that differential architecture of nuclear envelope proteins in cancer cells** can modulate the cellular signalling and promoting a pathological phenotype.

In the proposed project, using two- and three- dimensional cell culture systems combined with quantitative imaging, I would like to study the composition and architecture of nuclear envelope proteins and the consequences of their altered architecture in normal and prostate cancer cells. With the combination of classical molecular biology with bioengineering techniques and advanced imaging, **I would like to investigate how the composition and the architecture of the nuclear envelope can influence prostate cancer progression,** including the loss of cell's apico-basal polarity, migration and, in consequence, its ability to detach from the primary tumor, survive in the bloodstream, and metastasize. Within this project, various clinical samples will be collected including circulating tumor cells and primary prostate tumors. This clinical material will allow me to evaluate a possible correlation between the clinico-pathological parameters of and the degree of alteration of the nuclear envelope within the tumor.

This multidisciplinary project represents the **combination that connects molecular biology, quantitative imaging, and bioengineering with clinical pathology and translational oncology.** The results obtained within this project will influence the cell biology field by understanding the nuclear envelope architecture in cancer dissemination cascade. It could also potentially lead to identification of novel biomarkers of prostate cancer that, in the future, might facilitate diagnosis, prognosis and improve therapy of this disease.