

**Cancer Research Project 2018:**

## **Circulating miRNAs and cfDNAs as potential biomarkers for disease progression in (localized/non metastatic) prostate cancer after radiation**

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### **Responsability:**

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### **Background:**

Prostate cancer represents the most common visceral malignancy in men. While prostate cancer remains a potentially lethal disease, it represents a wide disease spectrum, particularly when low risk localized disease is diagnosed; with up to half of men may not need immediate intervention. On the other hand, men with higher risk localized disease need active treatment. Standard management options include radical prostatectomy, radiation therapy (external beam, brachytherapy). Over long years, the treatment choice has been a challenging question and mainly patient's age, life expectancy, the presence of significant comorbidities, and patient preferences. Although these risk stratifications are established tools in decision-making, they have many limitations. They predict neither treatment response nor disease progression. The variability of disease behavior, the cost and diversity of treatment options and the related impairment of quality of life have given rise to a need for a personalized approach. Recently, liquid biopsy biomarkers gained from blood have emerged as essential non-invasive tools for treatment and assessment. Such biomarkers are mainly investigated in the metastatic prostate cancer but not yet in the non-metastatic setting.

### **Research Question:**

To explore and identify non-invasive biomarkers in the non-metastatic prostate cancer setting which could be essential to identify patients most likely to benefit from a specific treatment (radiotherapy) leading to minimize harms and costs of ineffective therapies.

**State of Own Research and Planned Project:**

The Department of Radiation Oncology, at Inselspital, Bern in cooperation with the Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK) has launched a Swiss nationwide biobanking study named SAKK 63/12. Patient accrual along with biobanking started in 2012. In this study, blood samples are collected from different prostate cancer patients groups before treatment and regularly during follow up. More than 500 patient samples are available as yet. From those blood samples, different genetic biomarkers called miRNAs, and cfDNAs can be measured at different time points. The changes in these biomarkers in relation to radiotherapy could play a crucial role in management of future prostate cancer patients.

Over the last two years, we were able to evaluate the technical feasibility using pilot samples collected in the frame of the SAKK 63/12 study. In the preliminary results, we are able to identify miRNA changes related to radiation. The results of this feasibility phase are promising. These results will be presented in the next Scientific Association of Swiss Radiation Oncology meeting (August 2018) in Zürich.

We would like to extend our efforts in this interesting field. Our plan is to use a large number of the collected samples to validate and extend the previous findings allowing us to monitor real time changes in potential markers through survival time. We hope that through screening based on very traditional risk stratifications such as serum PSA, Gleason score and clinical stage along with considering both miRNA and cfDNA in blood in prostate cancer patients, our study will uncover vital information that can predispose patients who do not respond to treatment and eventually develop metastasis.

**Project Partners:**

- Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK)
- Department for BioMedical Research (DBMR), University of Bern
- Institute for Pathology, University of Basel
- Interfaculty Bioinformatics Unit, University of Bern

**Project Duration:** 3 years

**Project Milestones:**

<b>Project Milestones</b>	<b>Year 1</b>	<b>Year 2</b>	<b>Year 3</b>
Logistic preparation	x	x	
Continuation patient recruitment/followup	x	x	
Collection, retrieval and storage of samples, shipment of blood	x	x	
Next generation sequencing		x	x
Bioinformatics analysis		x	x
Clinical and bioinformatics data integration		x	x
Publications		x	x
Report submission to Funding organization	x	x	x

**Required Budget:**

Post-doc salary (70%)* remaining 30% salary is covered by internal funding.	203,700
Laboratory consumables	60,000
Sequencing of blood samples	120,000
Bioinformatics support	30,000
Publication, and dissemination of findings	12,000
<b>Sum</b>	<b>CHF: 425,700</b>