# **Exploring the Metastasis Process in Prostate Cancer using Interaction Networks**

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# **Motivation**

Prostate Cancer (PC) remains to be one of the leading causes of cancer death in North American men1. Metastatic events indicate the advanced stage of cancer and poor patient survival. Deeper insights in the pathways that cause a primary tumor to metastasize into distant sites are critical towards developing new biomarker and therapies and are clinically significant towards improving patient outcomes.

Conventional strategies use a single-gene approach where aberrant genes are considered independently from other genes. However, understanding the function of genes in a complex disease like PC requires investigation of genes within the context of their interaction networks (collectively called interactome)2. This idea is based on the observation that disease condition is characterized by aberrant networks of genes (subnetworks), which interact at the protein level or at the protein-DNA level.

OptDis algorithm3 has been reported to efficiently identify subnetworks with the best possible discrimination between tumour classes and provide better insights into the biological mechanisms. Our project aims to investigate differences in the transcriptome between primary tumors and metastatic tumors and biological pathways/function that could shed more light in the biology behind the metastasis process using OptDis.

# **Dataset:**

One of the major publications in prostate cancer, Grasso et al., 20124, has gene-expression dataset comprising of benign normal, primary and metastatic tumor samples from prostate cancer patient cohorts (Table. 1). All the metastatic tumor samples are from patient with castrate resistant prostate cancer (CRPC) which represent an aggressive type of PC that are hormone therapy or chemotherapy resistant. So while investigating the difference between the primary vs. metastatic tumors, our study might also be biased towards primary PC vs CRPCs.

**Details of the dataset**

* GEO Dataset ID: GSE35988
* Technology: Microarray
* Platform: Agilent Whole Human Genome Microarray (GPL6480 & GPL6848)

Table 1: Summary of the study design

|  |  |  |
| --- | --- | --- |
| Disease State | Number of Samples | Remarks |
| Benign Normal | 28 | 18 matched + 10 unmatched |
| * Matched Normal Samples: Normal samples matching to the patients with Primary Prostate Tumors * Unmatched Normal Samples: Normal samples matching to the primary prostate tumors included in the study but for which microarray gene expression profiles were not performed |
| Primary Prostate Tumors | 59 |  |
| Metastatic Tumors | 35 | All Metastatic tumors are CRPCs and are derived from various metastatic sites |

# **Project Scope**

**Milestone 1:**

* To investigate if there are some meaningful groups of samples that are clustered together representing a sub-type of the disease state.

**Milestone 2:**

* To discover subnetworks that can differentiate between the primary and metastatic tumors using OptDis.

**Milestone 3:**

* A subnetwork module represents the group of genes that are collectively differential but the individual genes within the subnetwork are not necessarily differentially expressed i.e. the subnetwork may contain genes differentially expressed at high levels as well as genes differentially expressed at low levels. The role of genes differentially expressed at low levels may be meaningful in the context of biological function and pathways.
* The above statement will be explored using t-test and accessing the p-values (or rank) for the gene in the subnetworks.

**Milestone 4:**

* To investigated the functional/pathway enrichment in the resulting subnetworks in relation to the metastasis events in prostate cancer.

**Milestone 5:**

* Biological interpretation of the results which can explain the metastatic cancer progression in prostate cancer.

**References**

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