

COVALENT HISTONE MODIFICATIONS

ON THE ANALYSIS OF

PROSTATE CANCER

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Bachelor's
Degree Final
Project

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EXPLANATORY VIDEO

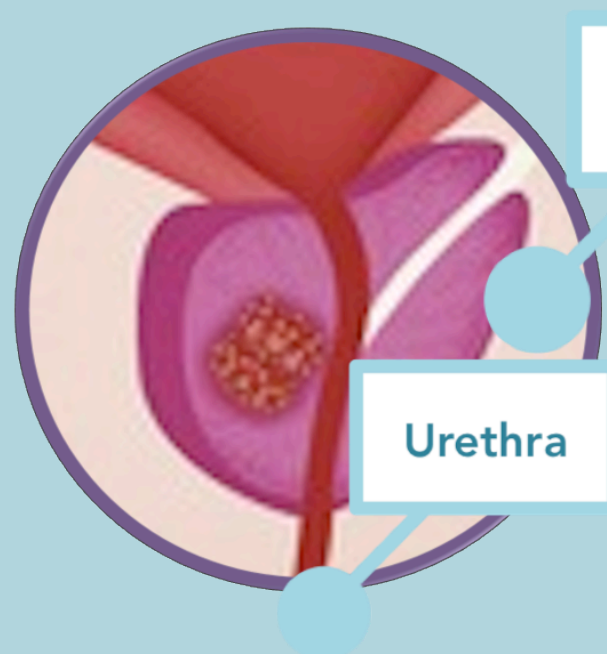
PROSTATE CANCER EPIDEMIOLOGY

Prostate cancer is one of the main reasons for men's death in civilized countries. It seems that incidence is not fully correlated with mortality rate and this is probably due to PSA screening methodologies.



The number of new cases detected, specially in North America and Australia, is growing dramatically.

WHAT IS PSA TESTING?



Prostate

Urethra

PSA is the acronym of "Prostate Specific Antigen". It is a serine protease synthesized by the prostatic gland that hydrolyses proteins from seminal coagulum when it passes by the prostate.

This allows liquefaction and expulsion of semen across the urethra. We can detect the PSA in a serum sample in low concentration. This concentration increases in prostate cancer, why this has been used so far to detect the pathology. However, this PSA increase can also be caused, for example, by a benign prostatic hyperplasia or by a prostatitis.

Is PSA screening a Good option?

APPLICATION OF

COVALENT HISTONE MODIFICATIONS IN PROSTATE CANCER

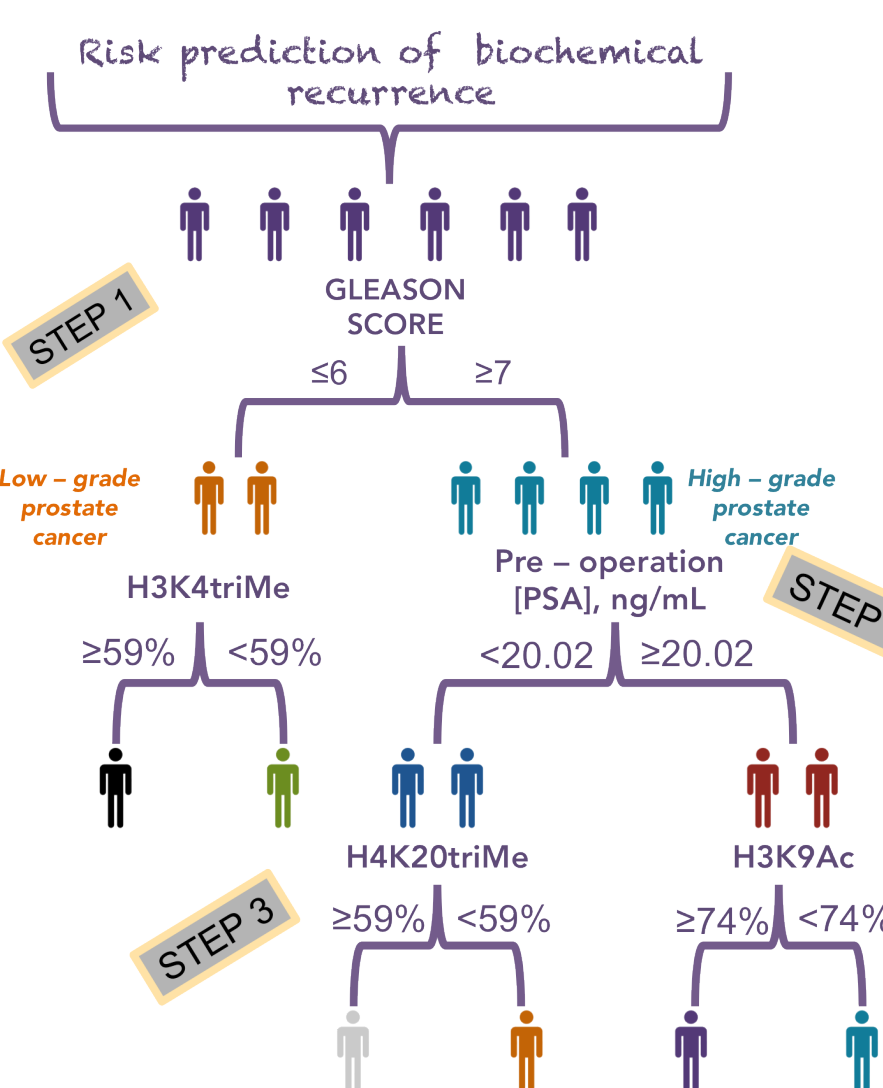
PROGNOSIS

DIAGNOSIS

THERAPY

After a primary tumour extraction, cancer patients have up to 50% chances for the appearance of a new tumour.

Nowadays, tumour characterisation is based on grade and stage scale to group patients with similar clinic – histological features. However, with different clinical outcome.

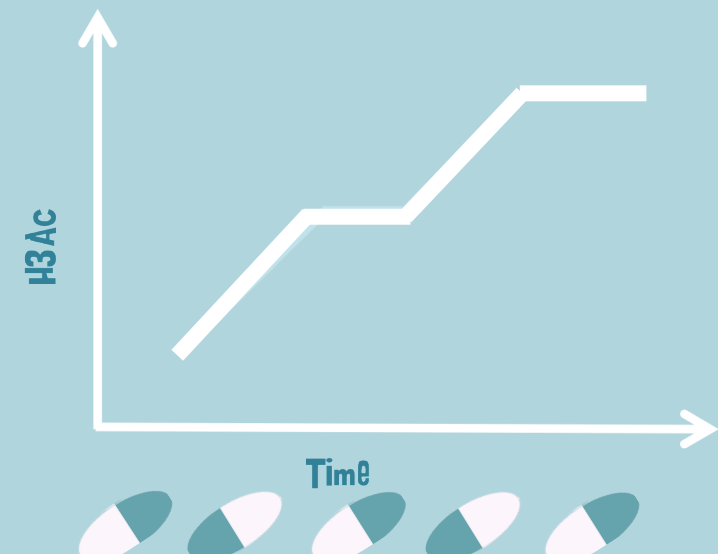


Histone modifications can improve this situation, because they allow calculating the risk prediction of biochemical recurrence after a primary tumour extraction. Then, we can group patients to obtain more accurate and cohesive clinical outcomes and this will improve the therapy.

Nowadays, there are different approaches that try to correct histone modifications patterns altered in prostate cancer. An example is the use of HDAC inhibitor. This drug allows to recover the level of acetylation, that is decreased in prostate cancer, because it inhibits an enzyme that remove acetylation from histones. Therefore improve the pathological state of prostate cancer patients.

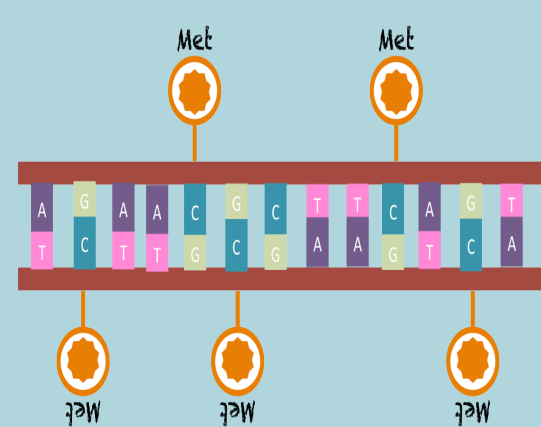


Prostate cancer patient



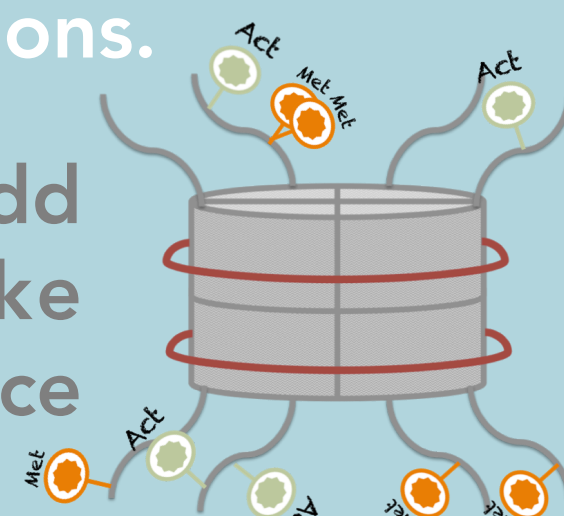
EPIGENETICS COULD BE THE SOLUTION

Epigenetics is the study of changes in gene expression that occurs without a change in the DNA sequence and are mitotically, and sometimes, meiotically heritable.

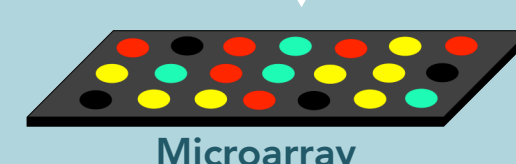
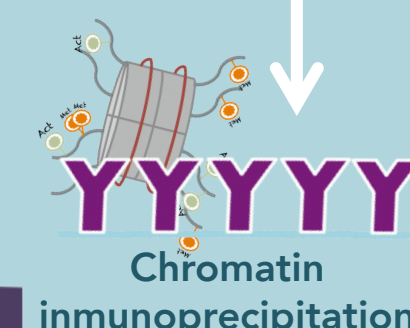


Examples of epigenetics mechanisms are DNA methylation of post - translational covalent histone modifications.

There are modifying – enzymes that can add or remove specific modifications, like methylation or acetylation. These take place specially at histone N – terminal.



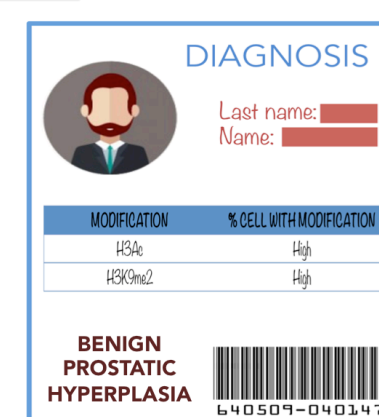
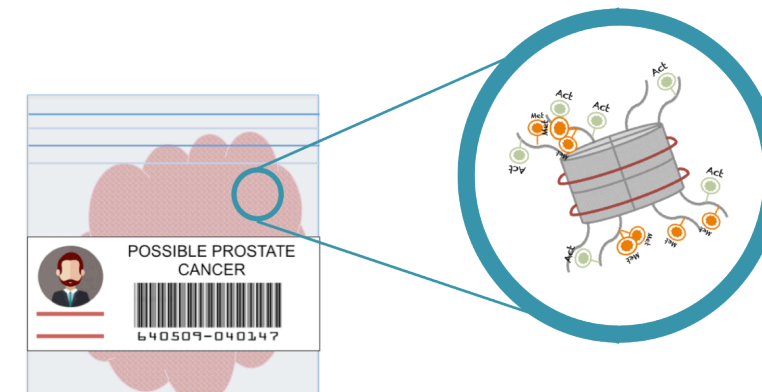
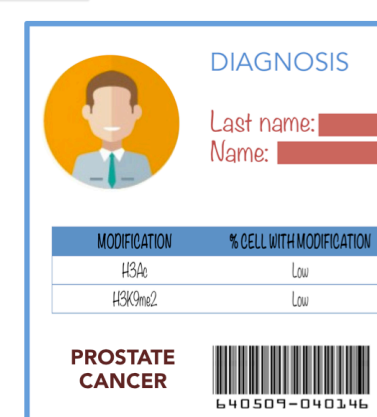
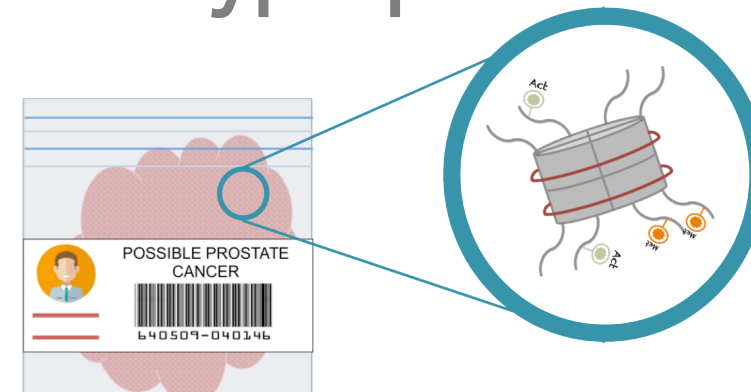
Histone modification can be mapped around the genome by Chip – on – Chip technique.



PSA testing cannot distinguish between a prostate cancer and a benign prostatic hyperplasia, but histone modifications can do it.

Histone modifications patterns are altered in the case of cancer. Then, when a patient has a low percentage of cell expressing specific modifications, we will diagnose prostate cancer.

If the percentage of cell expressing specific modifications is high, we will diagnose a benign prostatic hyperplasia.



Check it out here



Bibliography:

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Zhou LX, Li T, Huang YR, Sha JJ, Sun P, Li D. Application of histone modification in the risk prediction of the biochemical recurrence after radical prostatectomy. *Asian J Androl*. 2.010; 12: 171 – 179.