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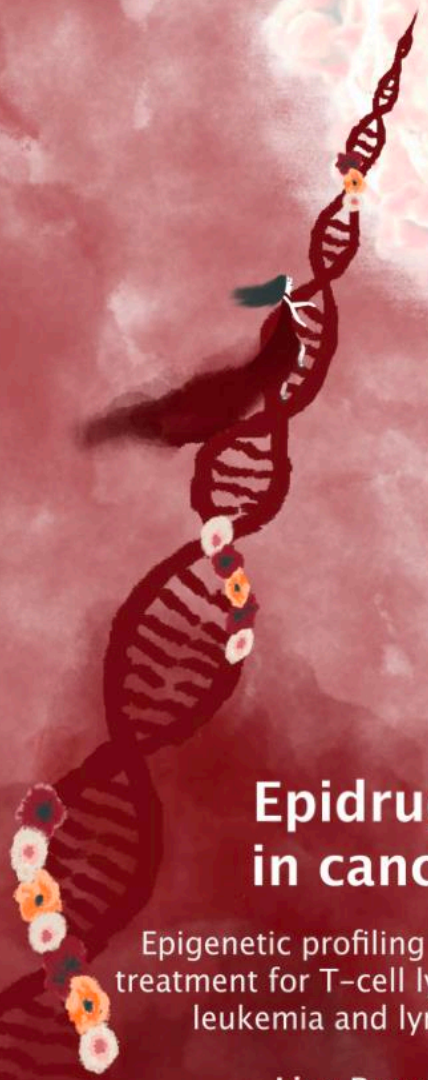

Epidrugs in cancer

Epigenetic profiling to improve treatment for T-cell lymphoblastic leukemia and lymphoma

Lien Provez

PHD DEFENSE
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Dissertation submitted to obtain the degree
'Doctor in Health Sciences'

My thesis in four simple questions and answers

1. Which cancer did you study?

During my PhD, I studied T-cell acute lymphoblastic leukaemia (T-ALL) and lymphoma (T-LBL), cancers caused by the body making too many T-cells. These rare, aggressive cancers occur mostly in children. The majority of patients (80%) can be cured thanks to chemotherapy and if necessary followed by bone marrow transplantation. However, this therapy causes various side effects and there is still a proportion of patients who do not survive the disease.

2. What exactly did you research?

Every cell in our body contains the same building plan, our DNA. Yet our cells get different functions by turning on and off different genes, pieces of our DNA. This is regulated by epigenetic mechanisms such as DNA methylation and histone modifications.

Epigenetics

DNA methylation is a chemical reaction in which a methyl group (CH_3) is placed on the DNA. Too much DNA methylation leads to the inactivation of tumor suppressor genes.

Histone modifications are changes that take place on the histones around which the DNA is wound. These modifications can affect the structure of the DNA and as such the activity of genes.

Cancer cells have defects in these epigenetic mechanisms that turn the wrong genes on or off. By understanding this better and resolving the mistakes with drugs, we hope to improve current treatment, thereby reducing the risk of side effects and death.

3. And did you find anything?

Yes! I found a drug, decitabine, that can eliminate excess DNA methylation in T-LBL which prolongs the survival of experimental animals. I also made an overview of histone modifications in T-ALL that can be used for further research to, for example, predict sensitivity of T-ALL patients to drugs.

4. Can physicians now cure all T-ALL and T-LBL patients?

No, not yet. The next step is to test decitabine on T-LBL patients before the drug can become part of the standard treatment. My research is just one small piece of an incredibly difficult puzzle. But with each puzzle piece, together we are slowly but surely building a world where cancer becomes a treatable disease.

Publications in this thesis

Pre-clinical evaluation of the hypomethylating agent decitabine for the treatment of T-cell lymphoblastic lymphoma.
Provez Lien et al. *Cancers*, 2023.

An interactive mass spectrometry atlas of histone posttranslational modifications in T-cell acute leukemia.
Provez Lien, Van Puyvelde Bart, Corveleyn Laura, Demeulemeester Nina et al. *Scientific Data,* 2022.

Additional co-author publications can be viewed on ORCID 0000-0003-2236-2347.

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My thesis and simple infographics

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