

PhD candidate in the spotlight:

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My name is Eva De Smedt and I have been working for the research group Hematology and Immunology ever since completing my master thesis in this lab in 2013. My research focusses on exploring the underlying anti-myeloma mechanisms of epigenetic agents, under the supervision of Prof. Dr. Karin Vanderkerken and Prof. Dr. Elke De Bruyne. Since October 2016, I am also the new teaching assistant for the courses 'Experimentele cellulaire en moleculaire biologie I' and 'Experimentele cellulaire en moleculaire biologie II' (under the supervision of Prof. Dr. Karin Vanderkerken and Prof. Dr. Ron Kooijman).

Multiple myeloma is a plasma cell malignancy that mainly resides in the bone marrow. Despite the introduction of novel agents, virtually all patients still relapse and develop non-responsive disease, hence the need for new treatment options. Next to genetic defects, studies indicate that epigenetic changes play a major role in MM pathogenesis. The best studied epigenetic modifications are DNA methylation and post-translational histone modifications (PTMs) like acetylation and methylation. These epigenetic modifications co-operate intensively to control chromatin compactness and thus gene expression. In cancer, the epigenetic landscape is completely disturbed. Intergenic regions are often hypomethylated leading to genomic instability, while promoter-associated CpG islands of tumor suppressor genes are instead hypermethylated and/or deacetylated leading to a loss-of-function. Of interest, these epigenetic aberrations are, in contrast to the genetic alterations (e.g. chromosomal translocations), reversible and thus present interesting new targets for therapeutic intervention. Two main classes of anti-cancer agents that target the epigenetic regulation of gene expression are the histone deacetylase (HDAC) and DNA methyltransferase (DNMT) inhibitors.

However, during my PhD, it has become increasingly clear that mutations and/or aberrant expression of HMTs also play a crucial role in MM pathogenesis. Therefore, our focus has shifted towards these

epigenetic modifiers and the evaluation of recently developed HMT inhibitors in MM therapy. Exploring combination strategies could decrease toxicity issues, a side effect which often occurs with the use of pan- HDACi and pan-DNMTi.

Have there been times where your research wasn't really working out the way you expected it to be? How did you cope with this difficulty? Or: What kept you motivated to continue nevertheless.

We just recently published a paper that was 4 years in the making. It was a real struggle to come up with different approaches in our attempts to explore underlying mechanisms of action. Dealing with rejections from journals was not always easy. I found it really useful to be able to discuss some of the problems we encountered and possible approaches with fellow PhD students from other labs, who master different techniques. I also had many discussions with my supervisor and colleagues from my own lab and this ultimately led to a better manuscript. In my opinion, the support of your fellow PhD students is really important to keep each other motivated.

Do you have a healthy work-life balance? If so, could you share the secret ingredient(s)?

It is not always easy to separate work from your private life. Especially when you are getting stuck and you're constantly thinking about possible solutions or new experiments that might bring you some answers. I like working with a to do list, so that I can maintain an overview of my work. During busy periods, I might need to work during weekends in order to meet a deadline. On the other hand, during quieter periods, when I have more free time, I also try to enjoy it and fix a lunch date with friends. In the beginning of my PhD, I had lots of ideas and planned a lot of experiments without thinking it through. I've learned to better design the experiments and define proper strategies in order to generate better results. Recently I became a mother, which does impact my work-life balance. I will try to stay organized and be efficient in the lab so that I can also focus on my personal life.