How would you explain the main findings of your paper to non-scientific family and friends?

We wanted to investigate the development of papillary thyroid cancer (PTC), the most common type of cancer in the thyroid gland. In many cases PTC is caused by a specific mutation called BrafV600E, which allows thyroid cells to divide uncontrollably and, eventually, form a tumor. We used an existing mouse model of PTC in which this mutation is activated only in the thyroid gland. We discovered a way to use this mouse model, such that only a few of the thyroid cells activate the mutation. We then followed and characterized the tumors that arise at different stages, and found different subtypes of PTC developed and that the tumors developed in a more or less normal microenvironment, with maintained thyroid hormonal function. When we use the mouse model in this way, it resembles human PTC in a more realistic way than previously used in vivo models.

What are the potential implications of these results for your field of research?

This mouse model could be used in so many ways! It provides the possibility to study very early events in cancer development, already before there are proper tumors. Thus, it provides a platform for testing different treatments at different tumor stages. One really important thing is that the model makes it possible to study the interactions between a tumor and its microenvironment. We know that the tissue surrounding a tumor has both tumor suppressing and tumor enhancing capabilities – involving, for example, different immune cells and fibroblasts – and that these interactions are most-relevant when investigating treatment-resistance mechanisms.

In human PTC, the majority of patients are women, and in our research using this mouse model we distinguish between female and male mice. By addressing the gender aspect, we hope to gain a better understanding of the hormonal mechanisms that are important for PTC.

What are the main advantages and drawbacks of the model system you have used as it relates to the disease you are investigating?

The mouse thyroid is very similar to the human thyroid, and the mouse genome has been studied in detail. Since this is a transgene mouse model, the animals are immunocompetent – a great advantage compared with, for example, a patient-derived xenograft model with immunocompromised mice. However, this means that we are not actually studying human PTC, but the mouse equivalent. Another drawback (or not?) is that we cannot fully control the extent of the mutation in the thyroid tissue. All mice develop tumors, but the pattern and tumor burden are very heterogeneous.

What has surprised you the most while conducting your research?

EJ: It was surprising to see that we could find signs of tumor development so early in the mice. It was also surprising that most of the mice seemed unaffected by the tumors. It was almost a bit creepy to work with mice that seemed perfectly healthy while knowing that they had tumors slowly growing in their thyroids.
ES: I was amazed by the fact that the mice managed to remain euthyroid despite a, sometimes high, tumor burden. It was also intriguing to observe the great heterogeneity in the phenotype, considering all mice harbor the same mutation.

Describe what you think is the most significant challenge impacting your research at this time and how will this be addressed over the next 10 years?

Conducting animal research is expensive and time-consuming, and using this mouse model with a heterogenous phenotype makes it harder to draw conclusions and perform quantitative measures. However, this unbiased way of evaluating tumor development by using transgene mice is, to our belief, more accurate in an era of more-personalized medicine. Implicating more non-invasive techniques of monitoring tumor growth and treatment response can be a tool when working with these animal models.

What changes do you think could improve the professional lives of early-career scientists?

No matter how hard we try, we cannot invent all wheels by ourselves, even as scientists. The importance of facilitating and enhancing networking, to have other persons around you with different abilities, different perspectives and adding new ideas – this cannot be overstated. We were lucky to do our PhDs in a group offering great possibilities, to take different courses and go to conferences meeting people able to help to understand our own research within a broader context. Not everyone has that privilege.

What’s next for you?

ES: I am writing my doctoral thesis and will defend at the end of this year. After that I will continue the research in Mikael Nilsson’s group, using mouse models and human material. I will also start to work clinically as an MD.

EJ: Since I finished my PhD project in Gothenburg, I have started working at the University Hospial in Linköping, Sweden. I’m currently a resident physician in oto-rhino-laryngology and work to become a specialist in that field. In parallel, I have taken up a postdoctoral position in Karin Roberg’s group in Linköping, where I work with other types of tumor in the head and neck region. But I also keep the contact with Mikael Nilsson’s group in Gothenburg. There are still a lot of data from my PhD project that are not-yet-published, and we are currently preparing two other articles concerning different events during the embryonic development of the thyroid gland. A final statement in my doctoral thesis was that there is still a lot of work to be done – and that is forever true.

Reference