'No nonsense research at the beach; Defining the rules of nonsense-mediated mRNA decay in human cancers.’ – Rik Lindeboom

At the end of last year I went to Spain for an eight month internship at the Centre of Genomic Regulation in Barcelona. While educated as a ‘wet-lab’ biologist, I became fascinated with computational biology during my previous internships and decided to join a computational lab for my final masters internship. Through the network of my former supervisor, I was very lucky to get an internship position in the prestigious laboratory of Prof. Ben Lehner. Here, I used The Cancer Genome Atlas (TCGA) data to elucidate the ‘rules’ of nonsense mediated mRNA-decay (NMD). NMD is a surveillance pathway that targets mRNA transcripts that bear a pre-mature stop codon (PTC) for degradation. PTCs can arise from mutations and cause protein translation to terminate pre-maturely, leading to incomplete and potentially toxic proteins. NMD often recognizes these transcripts and degrades them, but it is not completely understood when and why it sometimes fails. Since one-third of all genetic diseases - including many cancers - are caused by PTC inducing mutations, it is of great importance to understand why some of these mutations can evade this protective surveillance mechanism. I analyzed mutation and expression data of over 6000 cancer patients from the TCGA consortium and used machine learning to understand why some PTCs are not recognized by NMD. This analysis validated known and revealed several new ‘rules’ for PTC detection by NMD, which we can use to correctly predict NMD in more than 75% of the cases. When I got back in the Netherlands I wrote a manuscript and I’m very excited to announce that in the upcoming weeks we’ll submit this story to Nature Genetics with me as the sole first author. Overall, I’m extremely happy with the things I learned and the paper I merited during these months and I’m in good faith that this internship will help me in my future career in academia. In addition to my internship, Barcelona too treated me so, so good. In a pretty but vibrant city where the sun always shines, the enormous international community made it easy to make friends, and before I knew it I was going out every day of the week, being a young tourist for eight months in my own city. From longboarding down the Montjuïc and waking up on the beach after never-ending beach parties, to the excellent science at the CRG, it was all part of one of the best experiences for me so far.

