

## Early Career Researchers in the Spotlight

In the *ECR in the Spotlight* series, we highlight early career researchers recognized with notable awards. This time, we are turning the spotlight on two award winners presented at the NVVI Annual Meeting 2024. Meet **Christianne Groeneveldt**, winner of the 2024 Van Bekkum Thesis Award, and **Dennis Hoving**, awarded Bright Spark in Immunology 2024. They share more about their research, what drives them, and their vision on science.

### CHRISTIANNE GROENEVELDT

Postdoctoral researcher at the Department of Pulmonary Medicine, ErasmusMC.

[C. \(Christianne\) Groeneveldt, MSc, PhD - Researcher - Erasmus MC](#)

[www.linkedin.com/in/christianne-groeneveldt](http://www.linkedin.com/in/christianne-groeneveldt)

### Research for which the prize was received

During my PhD at the Leiden University Medical Center, conducted within the Department of Medical Oncology under the supervision of Dr. Nadine van Montfoort, Prof. Dr. Thorbald van Hall, and Prof. Dr. Sjoerd van der Burg, I explored the immunostimulatory potential of oncolytic reovirus for cancer immunotherapy. Many solid tumor types often show limited responses to

T-cell-based immunotherapies, largely due to a lack of intratumoral T cells. Using various preclinical tumor models, we demonstrated that treatment with oncolytic reovirus led to targeted infection and localized inflammation within the tumor, resulting in rapid and robust infiltration of (mostly reovirus-specific) CD8<sup>+</sup> T cells. These immunostimulatory characteristics of reovirus could be exploited using various therapies (synthetic long peptide vaccination, CD3-bispecific antibodies, or immune checkpoint inhibitors), leading to strong anti-tumor responses. We additionally found that the effect of some of these combinatorial strategies could be further enhanced by blocking TGF- $\beta$  signaling. Lastly, we showed that approximately 80% of individuals possess pre-existing reovirus-specific neutralizing antibodies, but their presence does not compromise the therapeutic efficacy of reovirus-based combination treatments.

### What made your research unique?

In recent decades, research on oncolytic viruses has primarily focused on their oncolytic function (i.e. their ability to directly lyse tumor cells). However, a comprehensive understanding of their immunostimulatory properties and how to harness these for therapeutic purposes has been limited. Our work with oncolytic reovirus has contributed several key insights with direct relevance for clinical translation. Notably, we demonstrated that the majority of T cells infiltrating tumors following reovirus treatment are not tumor-specific, but virus-specific. Importantly, we were the first to show that these virus-specific T cells can still be effectively redirected against tumor cells using CD3-bispecific antibodies. In addition, we challenged a long-standing assumption in the field that reovirus-specific neutralizing antibodies are beneficial for therapy. Our findings indicate that these neutralizing antibodies are not beneficial but instead impair the oncolytic capacity of reovirus. However, they do not prevent immune activation within the tumor microenvironment. Together, we presented compelling evidence that the immunostimulatory effects of oncolytic viruses are as important for their clinical benefit (if not more so) than their direct tumor-killing abilities.

### What do you see as the biggest challenge in immunology?

I think one of the biggest challenges in immunology is learning how to manipulate the immune system precisely without causing unwanted side effects. In cancer immunotherapy, for

example, the goal is to activate the immune system to recognize and eliminate cancer cells. However, pushing it too far can lead to serious complications, such as autoimmunity or excessive inflammation. Finding the right balance is incredibly difficult, especially because this balance could be different for each patient. Figuring this out requires preclinical models that properly reflect human immune biology, and the lack of those is another challenge in immunology.

### **What is your most important advice to young immunology researchers?**

Get good at visualizing your data, ideas, and mechanisms! The little details make a big difference, and if you can turn a messy concept into a clear figure, you probably actually understand what you're talking about.

### **How do you take care of a good work-home balance?**

To be honest, I might not be the best person to answer this question. I did not have a good work-home balance during my PhD. I spent long days in the lab, and work was my main focus (which I was okay with at the time). I have noticed that changing this way of working is quite difficult. However, I'm trying to be more conscious about setting priorities, realizing that not everything needs to be done right away, and that it's sometimes okay to delegate things to team members. And of course, allocating time for hobbies and seeing friends and family is also a nice way to recharge!

*Interested in learning more about Christianne's research? You can read her full thesis at <https://scholarlypublications.universiteitleiden.nl/handle/1887/3663612>*