

# INTERVIEW



**5X CARDINNOV**

ERA4HEALTH  
PROGRAMME

## *5x CARDINNOV*

Five projects involving CARIM researchers have been awarded a grant within the ERA4Health programme CARDINNOV: 'Research targeting development of innovative therapeutic strategies in cardiovascular disease'. The ERA4Health partnership is a European partnership within the Horizon Europe programme for innovative treatments in the field of cardiovascular disease. The partnership aims to fund international research in the areas of cardiovascular disease, nanomedicine and nutrition, health and prevention, over a seven year period.

## GENETIC CHANGES IN THE BLOOD

Dr Job Verdonschot, researcher and trainee clinical geneticist, is going to investigate the genetic changes in blood cells in order to improve the understanding of heart failure. Heart failure means that the heart no longer manages to adequately pump the blood throughout the body. He investigates how changes in these genes contribute to an inflammation in the body which ultimately affects the cardiac muscle. As Job explains: “What we see is that patients with heart failure often have a latent inflammation, but as yet we know little about the causes. Recent research found that changes in the genes of blood cells might play a role. Although such genetic changes occur in many people without causing problems, we think that major changes cause inflammations and so are part of the disease mechanism.” Job will therefore use a large database of patients with diastolic heart failure to investigate how frequent these genetic changes are. He will also examine the inflammation in mice with this genetic change. “This way we hope to find out whether anti-inflammatory drugs could help to reduce symptoms in people with this mutation in their blood cells and slow down the deterioration due to their heart failure, and what anti-inflammatory drugs we should use.”

## VARIOUS TYPES OF INFLAMMATION

Dr Vanessa van Empel, cardiologist and researcher, will be investigating how heart failure can be prevented or slowed down. She too will look at the role of inflammatory reactions. “What we want to know is whether there are subgroups of patients each with their own inflammatory mechanism, and whether this affects the way the heart functions. If the inflammatory reactions differ, the treatment effects may also differ. Vanessa previously set up a large cohort and database containing data of patients with heart failure, for the purpose of scientific research. It is this database that Job

hopes will provide answers to his research questions as well. Both Job and Vanessa will collaborate in these projects and will now be further expanding the database: “We will be inviting back all patients in our database and collect blood samples from them. We will extract the white blood cells from these samples to further investigate the inflammatory reaction.” The ultimate goal is to find a better way to treat heart failure.

## ENABLING THE CARDIAC MUSCLE TO REPAIR ITSELF

Prof. Leon de Windt, professor of molecular vascular biology, aims to help the cardiac muscle repair itself after a heart attack. “In a heart attack, the cardiac muscle gets damaged because it doesn’t receive enough oxygen, which is usually due to a blocked blood vessel”, explains Leon. “The problem is that the cardiac muscle cannot repair itself, which means that a heart attack causes permanent damage to the heart. But some animals, such as zebrafishes and African spiny mice, do have this ability.” Leon will try to understand which genes are responsible for this ability of the cardiac muscle to repair itself. He wants to use this knowledge to develop a gene therapy and find out if this can improve the natural capacity of the human heart to repair itself. He is going to test this on organoids, small versions of the human heart developed from human stem cells, as well as on thin slices of human cardiac muscle tissue.

## SUDDEN EXACERBATION OF HEART FAILURE

Dr Miranda Nabben, assistant professor specialising in cardiac metabolism, is concentrating on the treatment of sudden exacerbations of heart failure. If patients with heart failure feel symptoms like dyspnoea rapidly worsening, this is called acute decompensation of the heart failure. These people often need to be admitted to hospital, but there is as

yet no effective treatment available. That is because the cause of the exacerbation is unclear, although there are some indications. As Miranda explains: "It seems that changes in certain metabolic proteins play a major role in the exacerbation of heart failure. A new drug that counteracts these changes has been shown to improve cardiac function in test animals." Her research on rats with heart failure focuses on understanding the disruptions in these proteins. "We first want to understand the way the disease develops and find out how drugs can counteract these changes. We do this at various moments in time, to determine when the treatment is most effective." In addition to her research on rats, Miranda also uses organoids to study heart failure in human cells. "This way we hope to find a drug that can reduce the exacerbation of heart failure."

## RESTORING THE DISRUPTED INFLAMMATORY RESPONSE

Dr Marleen van Greevenbroek, medical biologist and epidemiologist, will investigate how the body restores its balance after an inflammatory response. A latent inflammatory response appears to play a part in people who, despite being effectively treated for risk factors like hypertension or a high cholesterol level, still develop a cardiovascular disorder. "Although there are drugs that can reduce the inflammatory response, thereby preventing or repairing vascular damage, they can increase the risk of infections", explains Marleen. "That's why we don't focus on suppressing the inflammation, but on resolving the inflammatory response after it's done its job." To this end, she investigates special compounds in the blood that promote the restoration of balance after inflammations. These substances are called 'specialised proresolvin mediators'. "Using data from The Maastricht Study, we aim to find out whether people who have higher levels of these

substances in their blood are at lower risk of cardiovascular disease. We also investigate whether genes that are involved in the production and functioning of these substances, influence the risk of cardiovascular diseases." Understanding the mechanism the body uses to resolve an inflammatory reaction can help to further reduce the risk of cardiovascular disease.

*ERA4Health promotes international research by granting subsidies to European partnerships, including those in the field of cardiovascular disease.*