

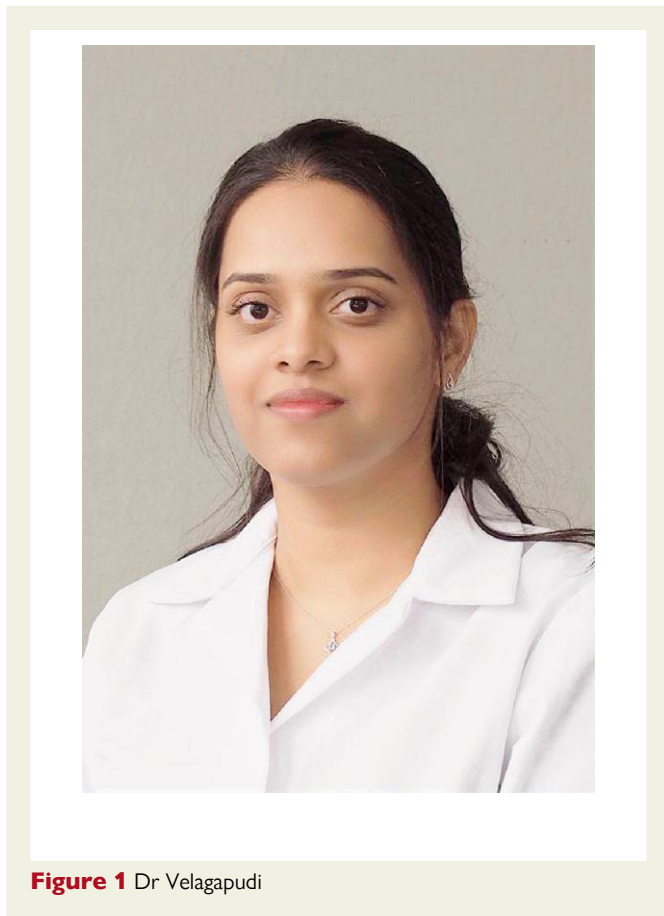
Rising Stars

Rising stars in cardiology: Srividya Velagapudi

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Srividya Velagapudi, PhD, is a molecular biologist who has been investigating aging, cardiovascular disease, and endocrinology for over a decade. Her outstanding work on Sirtuin-1, and low-density lipoprotein metabolism, earned her the Young Investigator Award in Basic Science in 2023. She is a senior researcher at the Center for Molecular Cardiology of the University of Zurich, Switzerland.



Dr Velagapudi's interest in science developed early as a school pupil in her native India when she found herself asking the question 'why' about the world around her. This early scientific curiosity was nurtured by her mother and two teachers Mrs Jayanti and Mrs Dhanalaxmi in particular. She says: 'Between the ages of 10 and 13 they helped me cultivate an interest in how and why things happened. They encouraged me to participate in scientific events and competitions and exposed me to early research which helped me develop a taste for science.'

She qualified in India as a basic biologist and then undertook further training in Switzerland at the University of Fribourg before completing her PhD in the lab of Prof. von Eckardstein and Dr Lucia Rohrer at the University Hospital Zurich (*Figures 1* and *2*). Vascular biology and ageing—areas that continue to engage her interest—became a focus of investigation while she was studying for her master's. Dr Velagapudi has been in her current role at the Center for Molecular Cardiology of the University of Zurich in the lab of Prof. Thomas F. Lüscher for over five years. Alongside her school teachers, she recognizes Prof. Lüscher as someone whose influence and guidance have been pivotal to her professional development.

As a basic biologist, Dr Velagapudi has a distinct sense of her role and responsibilities in scientific research. She values collaboration with clinicians for validation and the sense of perspective that they bring to her work, but also notes the differences in their approach and outlook. 'When I work on the bench, I am focused on the particular molecular mechanism in front of me and I may not immediately be looking into the therapeutic possibilities of that. Clinicians are valuable in helping to gain insights about how aspects of your work could be translated into having a clinical significance. I don't see this as a challenge, but as an opportunity to create a working environment where there is a healthy balance between basic researchers and clinicians who give



Figure 2 Dr Velagapudi and Prof. Thomas F. Lüscher

you a translational perspective to your work and look for potential therapeutic development.'

The award-winning project entitled: Sirtuin-1 directly binds and deacetylates hepatic PCSK9 to inhibit low-density lipoprotein receptor degradation,¹ was recognized along with another project from the University of Zurich at the European Society of Cardiology (ESC) Congress in 2023. Investigations on Sirtuin-1 have been ongoing in Prof. Lüscher's lab for over a decade and the award-winning project investigated how Sirtuin-1 inactivates proprotein convertase subtilisin/kexin type 9 (PCSK9). 'The idea for us was to not only target the

systemic lipid burden, which is what PCSK9 inhibitors basically do, but also to target vascular inflammation, which they don't currently do. It was like using one arrow to shoot two birds by reducing the systemic lipid burden, as well as reducing the inflammation that is caused by PCSK 9 in the vascular wall. Using Sirtuin-1, we were able to demonstrate in mouse models, a reduction in LDL cholesterol levels and atherosclerotic inflammation, along with elucidating the mechanism of action involving Sirtuin-1 deactivation of PCSK9.' Dr Velagapudi followed on from this work with a project to understand how PCSK9 and Sirtuin-1 interact with each other.

Winning the Award for Basic Research was not only a vote of confidence but also a chance to spread the word. She says: 'This was a project that I worked on for over four years, starting as a post-doc. There were ups and downs because working on the bench is different in as much as you are not focused on clinical, or market needs so much. For a lab-based person to be able to take their research to the ESC Congress and present it in front of such a large audience where you have all the pioneers in cardiology, is not only a validation of the work you have done, but also an assurance that you are going in the right direction.'

Following on from winning the Award, Dr Velagapudi continues with her research alongside her teaching role which she enjoys. She is committed to continuing research that is meaningful and productive and is currently happy to work wherever she finds the opportunity. She says: 'As long as I have space in a lab, funding, and a good reason to do my research, it doesn't matter where I am. Alongside teaching and interacting with students, it's something that gives me a reason to get up in the morning feeling optimistic.'

Her advice for would-be basic scientists is to be prepared for the highs and lows which are the nature of this sort of work. Every day presents challenges which you must learn to live with, she says, and basic research is not suited to anyone looking for quick-fire solutions or instant results. 'When you have completed a project and it works out, you feel like the child who got the chocolate, but at other times you may feel down because things haven't ended the way you expected. We have all been to depressing places when things have not worked out, but it's important not to give up. If you have your hypothesis and stick to your plan, you will get there, although in basic science, the research journey is notably longer compared to clinical research, and it can take years of work going from cells to animal models before finding even small-scale validations. It's important to be able to carry on with optimism and collaborate with others to achieve meaningful outcomes.'

Skills needed to be a good researcher include proficiency in basic bench work. This is fundamental, requiring focused dedication and adherence to one's research plan. Expanding expertise through learning and collaboration enhances research capabilities and potential for success and it's essential to break out of familiar comfort zones by seeking new techniques and methodologies. Relying on a few well-known skills limits growth and opportunities for innovation, Dr Velagapudi suggests.

Commenting on the Award, supervisor Prof. Lüscher said: 'Aging and longevity genes and the molecular pathways they express modulating cardiovascular function and disease been a major focus of my laboratory in Zurich for the last 15 years and our strategy over that time has been to better understand the regulation and importance. Vidya is an exceptional researcher who is very good at deciphering and understanding molecular pathways. For this project, she dissected exactly how Sirtuin-1, interacts with islet cells, improving their function and protecting these cells from being destroyed in obesity induced diabetes.

Vidya is meticulous in her work and very good at getting right down into the mechanisms of things. This project delineated pathways that could be used therapeutically. Although proteins are not very useful as drugs because their absorption ability is very low, in principle the active side of this enzyme could be designed as a new target with a particular molecule that may be absorbable.

Vidya is one of two Young Investigator Award winning students from my lab, alongside Florian Wenzl who won in the Clinical Science category. These awards are well-deserved, and we are very proud of both of them.'

Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

Reference

1. Velagapudi S, Xavier Miranda M, Mohammed S, Kraler S, Robert J, Rohrer L, et al. Sirtuin-1 directly binds and deacetylates hepatic PCSK9 to inhibit low-density lipoprotein receptor degradation. *Eur Heart J* 2023;**44**:ehad655.3285. <https://doi.org/10.1093/eurheartj/ehad655.3285>