

## FIRST PERSON

# First person – Sandra Vidak

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Sandra Vidak is the first author on 'Nucleoplasmic lamins define growth-regulating functions of lamina-associated polypeptide 2 $\alpha$  in progeria cells', published in Journal of Cell Science. Sandra Vidak is a postdoctoral fellow in the lab of Tom Misteli at the National Cancer Institute, NIH, Bethesda, Maryland, USA, investigating how the impairment of protein quality control mechanisms contributes to the progression of the premature ageing disease Hutchinson–Gilford Progeria Syndrome (HGPS).

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

Within the past few years premature ageing disorders have become the focus of intense interest, not only due to their severity and rapid development, but also due to their remarkable resemblance to normal human ageing. One of the disease models is Hutchinson–Gilford Progeria Syndrome (HGPS), an extremely rare genetic disorder characterized by accelerated ageing in children. Classical HGPS is caused by a constant production of a protein called progerin, a mutant form of the lamin A protein that is present in the cell nucleus and provides structural and regulative function. Progerin induces numerous nuclear and cellular defects, but the molecular disease mechanisms are still poorly understood.

We have previously shown that nuclear protein lamina-associated polypeptide 2 $\alpha$  (LAP2 $\alpha$ ) is reduced in cells from progeria patients and that the loss of LAP2 $\alpha$  directly contributes to the proliferation defect observed in those cells. In this study, we show that LAP2 $\alpha$  can either promote or inhibit the growth of progeria cells depending on the levels of the normal lamin A protein present in the nuclear interior (known as nucleoplasmic lamin A). Progerin expression in the cells leads to reduced LAP2 $\alpha$  levels, but the nucleoplasmic lamin A protein is still present in the nuclear interior, causing initial hyperproliferation of the progeria cells. As the disease progresses, cells lose nucleoplasmic lamin A, which together with the loss of LAP2 $\alpha$  causes decreased proliferation. At this stage, addition of LAP2 $\alpha$  in the progeria cells becomes beneficial, leading to increased proliferation almost up to the level of normal cells. Interestingly, expression of progerin and reduced LAP2 $\alpha$  levels have been found to be reduced in the cells derived from healthy older donors, suggesting that progerin and LAP2 $\alpha$  may have an important role in normal human ageing.

### Were there any specific challenges associated with this project? If so, how did you overcome them?

One of the main challenges was to establish patient-derived primary cell cultures. In contrast to cell lines, primary cells are extremely sensitive, often requiring additional nutrients not included in classical media and a significant amount of optimization to find the best culture conditions. In primary progeria cultures the challenge is even greater since the cells start showing progeria



Sandra Vidak

cellular phenotypes very early, one of them being reduced proliferation and increased senescence. In addition, there is great heterogeneity between patient cell lines, as well as within the individual cell cultures, which need to be taken into account during analysis and data interpretation.

### “...seek projects that make [your] heart beat faster...”

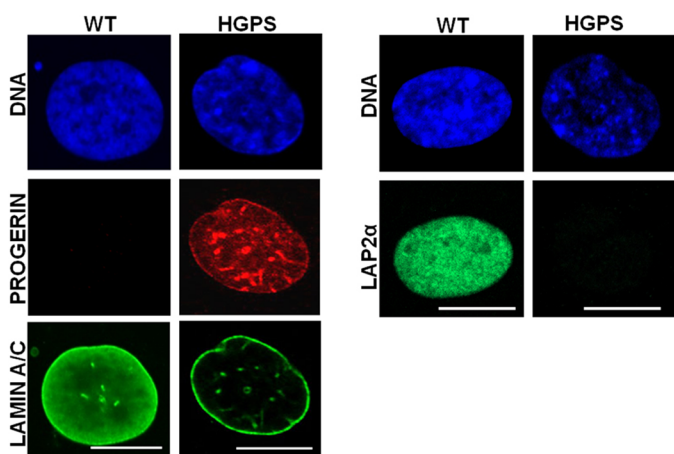
### When doing the research, did you have a particular result or ‘eureka’ moment that has stuck with you?

One of my ‘eureka’ moments was when we found that LAP2 $\alpha$  can affect proliferation of progerin-expressing cells in two different ways. We knew from our previous results that overexpression of LAP2 $\alpha$  reduces proliferation of wild-type cells through inhibition of the E2F-1 pathway, whereas in the progeria cells we observed two different behaviours upon ectopic LAP2 $\alpha$  expression: increased proliferation of cell lines showing a clear proliferation defect and reduced proliferation of cell lines growing at the same rate as the wild-type cells. This finding motivated me to dig deeper and find a mechanism behind this unusual behaviour. All the data pointed to the nucleoplasmic lamin A levels which, together with LAP2 $\alpha$ , have been shown to be important for the regulation of cell proliferation.

### Have you had any significant mentors, and how have they helped you?

Apart from my thesis advisor Prof. Dr Roland Foisner who has been a great mentor throughout my PhD and still continues to be one, I have to thank Dr Thomas Dechat who was a senior postdoc in the lab at the time of my PhD. He introduced me to the exciting world of

Sandra Vidak's contact details: National Cancer Institute, NIH, 41 Library Drive, Bldg 41, B513, Bethesda, MD 20892, USA  
E-mail: sandra.vidak@nih.gov



**Progerin expression causes loss of nucleoplasmic lamin A/C and LAP2 $\alpha$  in primary HGPS fibroblasts.**

progeria research and had a pivotal role in my pursuing a scientific career. I am grateful to both of them for giving me the freedom to follow my own ideas, yet always steering my research in the right direction. I am also grateful for an amazing PhD community consisting of numerous talented people with various scientific backgrounds who provided valuable input and support throughout my PhD career.

**“...a substantial part of a scientific career is being able to communicate your research to the scientific community.”**

#### **What's the most important piece of advice you would give first-year PhD students?**

In addition to choosing the right mentor, I would encourage new PhD students to seek projects that make their heart beat faster, cause excitement every time they get new piece of data and spark their curiosity. I would encourage students to network with as many different PhD students as possible because those are the people who can provide significant help with learning new techniques, give good scientific input, as well as provide emotional support. Because there will be days when nothing works, when you will not be able to confirm some exciting result, days when you will think that maybe you're not good enough or smart enough to do a PhD. And those

days are easier to go through if you have the right support and the right project. Also, a good work–life balance is crucial in doing a successful PhD; find something you like outside the lab and enjoy your free time.

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

One of the best opportunities for early-career scientists is being able to participate in various international conferences where they can present their data, network with scientists from their field and find new job opportunities. For that reason I think it is crucial to provide adequate funding that can support young people at the beginning of their career. In addition, I think the compensation and benefits early-career scientists are currently receiving need to be improved. Although we started this career for the love for science, it is imperative to provide good living conditions for scientists and their families.

#### **What's next for you?**

Since finishing my PhD, I joined the lab of Dr Tom Misteli at the National Cancer Institute in Bethesda as a postdoctoral fellow, where I continue to work on premature ageing disease. My major focus is to understand the effect of progerin accumulation and aggregation on protein quality control mechanisms and how the impairment in the specific pathway contributes to the progression of the disease.

#### **Tell us something interesting about yourself that wouldn't be on your CV**

During my PhD I discovered a passion for Zumba and Latin dance, which was the best way to unwind after a long day in the lab and to deal with stress that inevitably comes with doing a PhD. I was also part of the Vienna Biocenter Amateur Dramatic Club playing in our (in)famous Christmas plays that were always highlights of the year and the chance to end the year with laughter. This experience had a tremendous impact on improving my public speaking skills, an important trait for scientists since a substantial part of a scientific career is being able to communicate your research to the scientific community.

#### **Reference**

Vidak, S., Georgiou, K., Fichtinger, P., Naetar, N., Dechat, T. and Foisner, R. (2018). Nucleoplasmic lamins define growth-regulating functions of lamina-associated polypeptide 2 $\alpha$  in progeria cells. *J. Cell Sci.* **131**, jcs.208462.