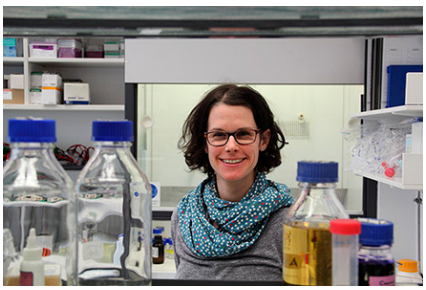
## Claudine Kraft: A hunger for understanding

Kraft's work focuses on the mechanisms that regulate autophagy in response to nutrient availability.



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**Claudine Kraft**

Growing up in Basel, Switzerland, Claudine Kraft attended a language high school with very little insight into the life sciences, but still found herself fascinated by mathematics, physics, chemistry, and cell biology. However, when it came time to decide what to study as an undergraduate, she couldn't make up her mind—every subject seemed too dry on its own. Following the advice of her volleyball trainer, she looked into biochemistry, a combination of the subjects she liked, and landed an internship in the group of Jeff Schatz at the Biozentrum University of Basel. Working under the tutelage of a patient and insightful graduate student by the name of Ursula Fünfschilling, Kraft was completely amazed at how biochemistry allowed her to "look" into the cell in an indirect manner, and by how many questions remained unanswered. She knew then that this was what she wanted to do—to understand the basic mechanisms of cellular life.

Kraft now operates her own lab at the Max F. Perutz Laboratories in Vienna, Austria. Her research focuses on the mechanisms regulating autophagy in response to nutrient availability. Work from her lab has elucidated the role of the Atg1 kinase complex, a sensor of nutrient signaling via the TOR (target of rapamycin) pathway, and other autophagic molecules in directing the activity of the autophagy machinery. We contacted her to learn more.

> "Science is not a job; it is a passion."

***Where did you study before starting your own lab?***

Following my internship with Dr. Schatz at the University of Basel, I attended the University as an undergraduate and received a degree in Molecular Biology. In my final year, I performed my one-year undergraduate thesis work in the lab of Dr. Stephen High at the University of Manchester, where I studied protein import into the endoplasmic reticulum in an in vitro reconstituted system. I went on to perform my graduate work in the lab of Dr. Jan-Michael Peters at the Research Institute of Molecular Pathology in Vienna, Austria, studying the regulation and substrate recognition of the anaphase-promoting complex in mitosis. My postdoctoral research brought me to the group of Dr. Matthias Peter in the Institute of Biochemistry at ETH Zürich in Switzerland. It was there that I began working on the selectivity and regulation of autophagy in yeast (1, 2).

***What was it that first drew your interest to autophagy?***

I investigated the cell cycle during my PhD. As this has been a highly populated research field for many years, many questions have already been answered, and many groups work in parallel on the same open questions. When I searched for a postdoc lab, I was fascinated by the field of autophagy, as it had gotten very little attention until that time, and therefore many very basic questions were and still are unanswered. When I joined the group of Matthias Peter, I was the first person there working on autophagy. I wanted to learn a genetic system but combine it with biochemistry, so this was a perfect match. Especially coming from the field of cell cycle and ubiquitin-dependent protein degradation, autophagy—another degradation pathway—fascinated me.

***What is your lab actively working on?***

In the lab we want to understand the basic mechanisms of autophagy, the cellular waste disposal system. Autophagy is an essential pathway during nutrient starvation and is also required to selectively eliminate proteins, protein aggregates, and damaged or excessive organelles. It has recently become evident that defects in autophagy are causally involved in numerous diseases, including cancer and neurodegenerative disorders such as Alzheimer's and Parkinson's disease. However, despite this intriguing medical potential, surprisingly little is known about the fundamental mechanisms.

Autophagy is regulated by the Atg1 kinase complex, which is itself under the control of the target of rapamycin (TOR) kinase. Together they act as the master regulatory system in autophagy. Several components essential for induction of autophagy have been identified, yet the mechanisms underpinning their mode of action remain elusive. Likely true for most biological pathways, we need to first understand the basic steps to then be able to intervene medically. Many approaches nowadays aim at identifying novel factors in certain pathways, but mostly we still don't really know *where*, *when*, and *how* the known factors act, and this especially is what we are aiming at in my lab.

Mechanistic insight into the function and regulation of the Atg1 kinase complex and the components of the preautophagosomal structure is key to understanding how autophagy is regulated. Our goal is to analyze the architecture, regulation, and function of the Atg1 kinase complex and to dissect the signaling events that induce autophagy. Along these lines we recently identified the first Atg1 kinase substrate in budding yeast called Atg9 (3) and identified a

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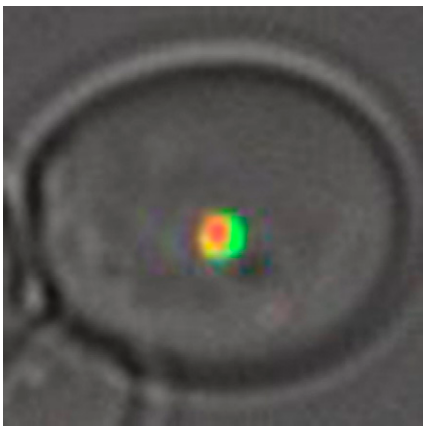

IMAGE COURTESY OF CLAUDINE KRAFT

**Yeast cell with an autophagic cargo (Aminopeptidase 1, red) being enwrapped by autophagic membranes (Atg8, green).**

new kinase acting in selective autophagy, the casein kinase 1 delta/epsilon homologue Hrr25 (4). We mainly use yeast as our model system but also test our insights using mammalian cells. We also use in vitro approaches to dissect individual steps in more detail. More recently we initiated synthetic in vivo approaches to understand the factors that are not only required for autophagy, but those that are sufficient. Our long-term vision is to reconstitute autophagy in a minimalistic system in order to understand in detail how Atg1 kinase and other key players in autophagy function. Our long-term goal is to understand the signaling events and the functions of individual components during the early steps of autophagosome formation.

***What did you learn during your PhD and postdoc that helped prepare you for being a group leader?***

I learned that science is not only about the individual in the lab, but that we need to work as a team, both during our daily work and when we interpret our results to come up with possible explanations, hypotheses, and models. It is important to have a team of people working together well, and that they enjoy what they are doing. Science is not a job; it is a passion. We have an absolutely fantastic team and great lab atmosphere with a lot of discussions and ideas, which creates a very creative environment. I strongly believe this is key to success, and I am very thankful for this fantastic group!

***Was there anything that you were unprepared for?***

I was unprepared for the different "psychology" of individual people in the lab. I was similarly unprepared for this when I had children, as in a way, it is quite similar. You have to find out which individual needs what kind of treatment and attention, and then try to provide it. And this is not always easy—not at home or in the lab.

***What have been your biggest accomplishment and challenge in your career so far?***

Surviving my first years as a junior group leader with two small kids, who were eight months and 3.5 years when I started. Managing family and science in parallel is still a challenge, and I would often like to split in half, but I consider my family my biggest accomplishment outside of the lab.

***Who were the key influences early in your career?***

Jeff Schatz and Ursula Fünfschilling, for the reasons described above. Then Steve High, my undergraduate research supervisor, who infected me with the enthusiasm of dissecting mechanistic steps in pathways. And Jan-Michael Peters, who was a great PhD supervisor; he was already letting me explore my own crazy ideas during the second half of my PhD, which was a great experience early on. And Matthias Peter, my postdoc supervisor; during my postdoc time I had two kids, and Matthias always gave me plenty of freedom and allowed me to handle family and science in my own way (with a water bath at home to grow my yeast cultures during the night). He had full trust that I would manage, and this was key for me to believe in myself and stay confident as a scientist and as a mother.

***What is the best advice you have received from your previous mentors?***

To quote Jeff Schatz: "Do things the way you do them and not the way everybody else thinks you should do them."

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***What are your hobbies?***

I enjoy climbing, mountaineering, and ski touring. These are similar to science, in that often you have to find another way which may not be the straightest way up, but you need to believe that you can do it such that you do not give up.

1. Kraft, C., et al. 2008. *Nat. Cell Biol.* 10:602–610.
2. Kraft, C., et al. 2012. *EMBO J.* 31:3691–3703.
3. Papinski, D., et al. 2014. *Mol. Cell.* 53:471–483.
4. Pfaffenwimmer, T., et al. 2014. *EMBO Rep.* 15:862–870.

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**Kraft and her family skiing.**