Professor Helen Blau, Director of the Baxter Laboratory for Stem Cell Biology at Stanford University in California, has spent her career studying cells and probing their plasticity. She does this in order to answer the fundamental questions that drive her research: how do cells develop from pluripotency to differentiated states, how do they maintain their identities, and can reprogramming alter those identities?

In the 1980s, as an assistant professor, Blau performed groundbreaking reprogramming studies showing that human cells thought to be terminally differentiated (hepatocytes, keratinocytes, and fibroblasts) could be directly reprogrammed to express genes of an alternative fate (muscle) without the need for DNA replication or cell division. She achieved this by fusing cells of 2 different fates together to form heterokaryons.1–4 Her work provided early evidence of the plasticity of adult differentiated cells and is widely viewed as a precursor to the techniques used to create induced pluripotent stem cells (iPS).

In addition to her heterokaryon work, Blau’s contributions to the reprogramming field and to molecular biology in general are numerous and diverse. She has shown that active DNA demethylation is critical to reprogramming cell fate,5 characterized muscle stem cells and their regulation in bioengineered stem cell niches,6,7 and studied their role in Duchenne muscular dystrophy,8 as well working on gene therapy strategies for promoting angiogenesis.9

Blau has achieved great success in her career and counts among her many honors election to of the American Academy of Arts and Sciences and the Institute of Medicine of the National Academy of Sciences, as well as fellowship in the American Association for the Advancement of Science.

She spoke to Circulation Research about the differences between men and women scientists, the importance of family, and how she still loves to be in the laboratory puzzling over cells.

Where Did You Grow Up?
I was born in London. I lived in the US until I was 6, then in Germany, and spent my summers in France and Switzerland. I pursued undergraduate studies in England before coming to the US at 21 to do a PhD at Harvard.

My father was Chief Historian for Europe for the US army and then a Liaison Office at the American Embassy in Bonn. My mother taught German language and literature.

Was It Hard to Be Moving a Lot?
It wasn’t easy in that I changed friends and locations so often, but in retrospect it was a blessing in disguise, because it made me very adaptable. I learned quickly how to deal with new environments and figure out the ropes, and I think that was an invaluable lesson in life: understanding how to relate to different people, countries, languages, and cultures.

I actually thought moving a lot was exciting. When I was about 9, my sister and I lived on a farm in Austria. I spent several summers at an international school, the Ecole d’Humanite, nestled in the Alps in Switzerland. When I was 14, I told my parents I wanted to learn French, so off I went, little dictionary in hand, to live with a French family, first in Brittany and then on the Cote d’Azur, absorbing the language, enjoying the dramatic tidal changes, riding a moped to photograph the countryside, and sailing into the sunset. Thus, I learned early the profound influence of the microenvironment.
You Went to York University in the UK. What Did You Study?
Biology. Actually, I wanted to study biology and linguistics, to combine arts and sciences, but rapidly found out that it was totally impossible in Britain; all the classes conflicted.

Was It Hard to Choose?
No. My teachers said, “Well, you’re good at arts and sciences, but you can always do art on the side, and you can’t do science on the side.” But of course, you can’t do anything on the side really well if you are fully into one career. It is all-absorbing.

As an undergraduate at York University, I did experiments on liver regeneration. To this day, we do not understand how the liver, the one organ humans regenerate well, is able to do so.

I loved doing research but always made time for other activities. I made a movie on sex education, was a regular at the pubs featuring a capella Irish ballads, enjoyed rubbing brasses of gallant knights with lions at their feet in remote village churches and exploring the moors—so I did do things on the side.

How Did the PhD Come About?
I got very excited about my research at the end of undergraduate studies, and so I went to my advisor and chair of the department, Ramsey Bronk, and asked him whether he would consider backing me for London or Edinburgh University. He said, “How about Cambridge or Oxford?” And then he said, “You know what, you should go to the US. Why not Harvard?” So he encouraged me and helped line up interviews.

I thought I would go for a year, earn an American degree (MA), and return to Europe. But when I got to Harvard, I was struck by the fact that there were endless opportunities, and one’s own imagination and energy were the only limits.

I worked really hard, but continued to pursue other activities—photography, skiing, and singing the blues and folk songs in a group named Free Energy (Delta G) at the Idler and NoName clubs in Harvard Square.

So You Stayed …
Yes, I found the US extremely exciting. Plus, I met my husband at Harvard. David is a research psychiatrist, so we often joke that he covers the mind and I cover the body.

Some men make it hard for women by expecting them to do everything: cooking, cleaning and child-raising. But David felt that my career was every bit as important as his and that we would do whatever we could to make it possible for me to pursue it fully.

He was pivotal to my success. He believed in me more than I believed in myself and always encouraged me. He would say, “You think like a cell. You have a special gift and you have to realize it.”

How Do You Encourage the Women in Your Laboratory?
I do something that wasn’t done for me, which is that I teach them all the tricks of the trade. Communication is critical to success. I teach them how to give good talks, how to write lucid papers and grants, and how to rebut. I give them opportunities to speak all over the world. So, when they come out of my laboratory, they hit the ground running. I have a good track record of successful women, and men, coming out of my laboratory who are professors at Harvard, Stanford, etc. They are confident; they are leaders. It is fun when I go to international meetings and my ex-trainees are running them. I take great pride and joy in the success of my scientific progeny. As often as not, they are women and have families. I think my example of doing both helped. When I had children, people said, “Oh, you’re not going to manage.” But I did. Luckily, times are changing, and the environment for women is much better, more conducive to combining career and family.

How Did You Juggle Family and Science?
It was always a dilemma. I never felt I did justice to the family or to my work. It was a complex juggling act. But one stimulated the other, and I think I was a better mother because I loved my work and a better scientist because I did not invest my entire life in my career. I always felt it made me more adventurous, more of a risk taker. I like to think I helped other women as a role model.

What Would You Say to Young Scientists Who Want to Start Families?
Don’t miss the chance to have a family. It is a source of enormous joy. I have 2 children. My son is a Harvard-trained architect, and my daughter is graduating from Yale law school; both are idealistic, compassionate, and determined to make a difference in this world. I learn so much from them. I think having a family allowed me to be more creative, daring, and bold, because my whole life was not focused on science; I had a balance.

What Are You Most Proud of in Your Career?
Challenging and changing dogma. Showing that the differentiated state, which was thought to be fixed, is actually reversible, dynamic, and continuously controlled by the balance of regulators (proteins, RNAs). I think that has changed the view of cell fate, how it is established, maintained, and altered. So, I’m finding our work in the 1980s has far broader implications than I realized, eg, in reprogramming toward pluripotency (iPS) and directed reprogramming, which is tremendously gratifying.

And What Was Your Lowest Point?
My father’s death about 12 years ago. He was very supportive of me. He had sparkly blue eyes, a wonderful way with words, a sharp mind, and a great sense of humor. He impressed on my sister and me the importance of knowledge and higher degrees, something no one could ever take away.

What Are You Working on These Days?
We’re using heterokaryons to elucidate mechanisms that could make reprogramming and regenerative medicine more effective, reliable, and efficient. Additionally, once pluripotent, cells must be redirected, and achieving a truly stable
differentiated state and avoiding cancer remains a challenge. Further mechanistic insights are crucial.

We’re also looking to other sources of cells for regenerative medicine, different ways to capitalize on cell fate reprogramming. We are using artificial bioengineered niches to exploit the tremendous potential of the muscle stem cells that exist in our bodies and are constantly enlisted to repair muscle damage. This platform is especially well suited to drug discovery. In addition, we are learning the secrets of the newt and ways to recapitulate in mammals the mechanisms these amazing creatures use to regenerate their limbs and hearts. This entails dedifferentiating cells by removing the brakes on the cell cycle, which allows cells of known identity to make more copies of themselves.

And we’re studying the etiology of Duchenne muscular dystrophy. A conundrum has been that mice lacking the same gene product as humans do not manifest the disease. We hypothesized that the basis might be telomere length, which differs between mice and humans; that appears to be the case. Our new mouse model that lacks dystrophin and has shortened telomeres recapitulates the human disease as its muscle stem cell reserve is depleted, suggesting new therapeutic strategies.

How Hard Did You, and Do You, Work?
I’ve always worked hard, and I still work extremely hard, even harder than ever. But that’s because I am excited about what we are doing, and I feel I can make a difference. Unexpected things happen in the laboratory weekly, we’re making new discoveries, and I’m having so much fun. I love my work. My team is an international group of highly creative scientists: my scientific children. One of the most gratifying things I do is training the next generation. In addition, I am now determined to bring our fundamental findings to the clinic through biotech and pharmaceutical companies and improve the quality of life for patients.

What Do You Think Are the Keys for Scientific Success?
Being bold and creative, taking risks, and challenging dogma. Creating a laboratory atmosphere that is conducive to discovery is important: a place where people have their own research domains but interact and help one another. The energy that comes from synergy is key.

Do You Ever Look Down a Microscope Anymore?
I do all the time. I still love looking at cells.

References
Helen Blau: She Thinks Like a Cell
Ruth Williams

Circ Res. 2012;111:672-674
doi: 10.1161/CIRCRESAHA.112.277863
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/111/6/672

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org//subscriptions/