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IN MEMORIAM

Margarete Heck (1959–2023): Cell biologist, geneticist, and incandescent social spark

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Margarete M.S. Heck, professor of cell biology and genetics, University of Edinburgh, died peacefully at home amid her loving family under a blue moon on August 30, 2023, after a long journey with ovarian cancer.

Margarete was born in Munich, Germany, on May 5, 1959, to Irina (1928–1980) and Dr. Heinz Hartmann Heck (1927–2002). She came from a renowned family of zoologists: her great-grandfather and grandfather were directors of the Berlin Zoo, while her uncle was the director of the Tierpark Hellabrunn in Munich. Margarete was 6 weeks old when her parents moved to New York State to live on the grounds of the Catskill Game Farm, the largest private U.S. zoo, where her father became director. She and her younger brother, Georg (1966–2018), enjoyed the zoo and the surrounding forests as their playground, laying the foundations for her enduring passion for biology.

Margarete attended the State University of New York (SUNY) Plattsburgh, where she initially studied medical technology but subsequently changed her major to microbiology, in which she excelled. In 1981, during her senior year, Margarete became the first student from SUNY Plattsburgh to be awarded a Fulbright scholarship, enabling her to spend a year using electron microscopy to study chromatin organization in *Chironomus* with Dr. Jan-Erik Edström at the European Molecular Biology Laboratory in Heidelberg.

While there, she decided to pursue a PhD in cell biology. She completed her graduate studies at Johns Hopkins University in Baltimore, working with Prof. Bill Earnshaw on the role of DNA topoisomerase II in chromosome structure and cell proliferation, and generating several highly cited publications (Earnshaw et al., 1985; Earnshaw and Heck, 1985; Heck et al., 1988; Heck and Earnshaw, 1986). Margarete and Bill subsequently were married at the Catskill Game Farm in 1988. Margarete was awarded a fellowship from the Jane Coffin Childs Memorial Fund for Medical Research to perform postdoctoral research at the Carnegie Institution for Science, Baltimore, where she worked with Allan Spradling from 1988 to 1992.

Margarete thrived at Carnegie. In a technical tour de force, she used 2D gel analysis coupled with microdissection to map an origin of DNA replication for the first time in an animal chromosome (Heck and Spradling, 1990). Driven by the pressing need to mutate and identify genes important for myriad cellular processes, she joined a 17-person team in the Spradling lab to carry out a powerful new type of *Drosophila* genetic screen, single transposon insertional mutagenesis, on the largest scale yet attempted. Margarete was one of the underbosses who, over an intense 4 months, helped dole out work assignments with characteristic kindness and humor, keeping everyone at a high level of enthusiasm. The resulting mutant collection jump-started her own research program on chromosome behavior during mitosis (Heck et al., 1993). Furthermore, she and the other screen workers generously donated all 1,000+ lethal mutations from the screen to the *Drosophila* Stock Center for free and immediate public distribution. The collegial nature of the *Drosophila* community was something Margarete enjoyed throughout her career, and she greatly valued helping to maintain that tradition.

Margarete Heck in academic regalia, University of Edinburgh, 2009. Photo courtesy of Allan Spradling.

Margarete established her own independent research lab as an assistant professor in the Department of Cell Biology and

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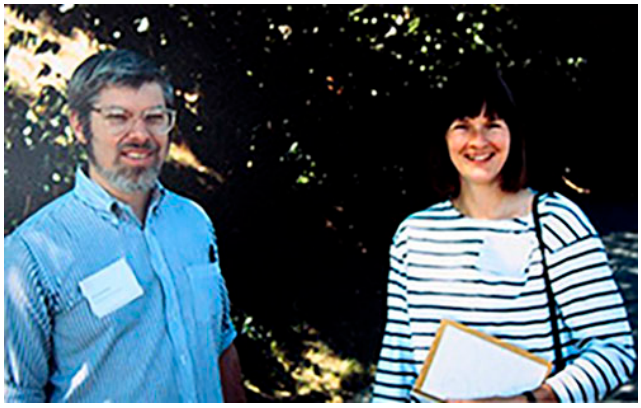

Margarete Heck with her postdoctoral advisor, Allan Spradling, at the Cold Spring Harbor Laboratory, 1989. Photo courtesy of Allan Spradling.

The Heck lab in 2009, depicting (from left to right) Sharron Vass, Margarete Heck, Neville Cobbe, Edward Duca, Ekin Bolukbasi, Ching-Wen Chang, and Francesca Di Cara. Photo courtesy of Sharron Vass.

Anatomy at the Johns Hopkins University School of Medicine (1992–1995), using her immunofluorescence microscopy skills in collaboratively exploring the mitotic function of an essential kinesin-like protein (Heck et al., 1993). During Margarete and Bill's time in Baltimore, they had two children, Charles (born 1991) and Irina (born 1993). Both went on to study medicine and were on the front lines during the COVID pandemic. They are also both on track to become fifth-generation Heck PhDs (Charles in melanoma immunology at the University of Manchester and Irina in radiation oncology at the University of Edinburgh).

Margarete and Bill were recruited to the University of Edinburgh as part of a drive initiated by Adrian Bird and the late Sir Kenneth Murray (1930–2013) to establish a center for cell biology there. The family moved to Scotland in 1996. They lived in a cottage amid scenic woodland and fields near Peebles, extending warm hospitality to family, friends, and visiting colleagues over many years. Margarete was initially awarded a Senior Research Fellowship by the Wellcome Trust (1996–2005), managing an active research lab in the College of Science and Engineering while also serving for many years as both program director for the Masters by Research in the Biomedical Sciences and deputy director of the pioneering Wellcome Trust 4-year PhD program in "The Cellular and Molecular Basis of Disease" (running one of the three modules of the program at the Wellcome Centre for Cell Biology). She continued to demonstrate both collaborative collegiality and independent novelty in the publication of highly cited papers analyzing conserved proteins for which *Drosophila* mutants displayed pronounced defects in chromosome condensation and segregation (Loupart et al., 2000; Warren et al., 2000; Steffensen et al., 2001; Cobbe and Heck, 2004), as well as characterizing a novel metalloprotease (invadolysin) that was found to link mitosis with cell migration (McHugh et al., 2004).

Margarete was then recruited to the University of Edinburgh's College of Medicine and Veterinary Medicine by Sir John Savill and John Mullins, supported by a Wellcome Trust University Award (2006–2011). She was attracted by the interdisciplinary nature of the Centre for Cardiovascular Science, and her work with *Drosophila* opened new opportunities for using model organisms in cardiovascular research. Here she continued to focus primarily on the mechanism of action of invadolysin, using both *Drosophila* and vertebrate models, provocatively revealing localization of the protein to the surface of intracellular lipid droplets (Cobbe et al., 2009) as well as demonstrating its essential roles in *Drosophila* mitochondrial function (Di Cara et al., 2013) and zebrafish cell migration (Vass and Heck, 2013). Her group also demonstrated a novel, unexpected role for an Elongator complex subunit in insulin signaling (Bolukbasi et al., 2012). Her research led to an active involvement with the international community of protease researchers, with invitations to talk at conferences around the world. She served on the council of the International Proteolysis Society and edited their newsletter "QuickCuts." Characteristically for Margarete, when she attended the International Congress of Cell Biology in Hyderabad in 2018, she agreed to give a careers lecture at a local teachers college, and was an immediate star, being featured in the local newspapers and television.

Margarete gained a Personal Chair in Cell Biology and Genetics at the age of 48 and became the first female professor in the Centre for Cardiovascular Science. The title of her inaugural lecture was "Time flies like an arrow, fruit flies like a banana," an homage to the Marx Brothers, reflecting her flair in mixing humor with a serious scientific focus.

Margarete was at once precise and analytical, and touchingly sentimental. Not only was she deeply devoted to her family (and justifiably proud of their achievements), but she cared enormously for all who worked with her, wholeheartedly encouraging them to do their best with integrity—regardless of the field in which they might ultimately find themselves. Margarete, indeed, was not only a scientific mentor but a life coach and a real friend for all her trainees, always ready to encourage and advise them in pursuing their goals. One of Margarete's recurrent and inspirational quotes was, "Nobody is going to take care of your career if not yourself." This advice has inspired many to persist and push and achieve their goals in their careers and beyond. Consistent with her enduring concern for the welfare of

Margarete Heck and Bill Earnshaw together. As Margarete wrote to her many friends in August 2021 (only months after the recurrence of ovarian cancer was diagnosed), "I thank my lucky stars every day for the many blessings of my life!" Photo courtesy of Bill Earnshaw.

others' careers, she participated in a Gordon Research Seminar career panel in 2014 and a GRC Power Hour in 2019 to address challenges faced by women in science (alongside issues of diversity and inclusion). Her collegiality within the wider UK cell biology community was abundantly evident in her sustained service as a BSCB Ambassador for the British Society for Cell Biology, as well as her co-organizing many highly successful conferences.

Indeed, Margarete's commitment to research student interests was evident throughout her long-standing capacity as postgraduate director for the Deanery of Clinical Sciences, providing enthusiastic and practical direct support for individual students, while also contributing constructively as a member of both the College Postgraduate Board of Examiners and the College Researcher Experience Committee. Even during her final stage with cancer, Margarete prioritized the ongoing support of her last PhD student through both thesis submission and the viva process (equivalent to a thesis defense), which was successfully completed only a week before her death. Strikingly, Margarete remained positive to the end, bravely and selflessly focused on trying to make things better for others while personally thankful for what she had.

On the day of her funeral (September 7, 2023), the flag of Old College, University of Edinburgh, was flown at half-mast as a mark of respect to Margarete, a gesture she would have been deeply humbled by. The funeral was a quiet family affair, and was officiated by the same humanist celebrant who had married Irina to Steve Lovejoy in a field above the house in May 2022. At that wedding, Margarete had asked the celebrant if she would officiate at her own funeral. A month after the funeral, a large number of friends, family, former doctoral students, and colleagues gathered at the Eastgate Theatre, Peebles, on October 22, 2023, for a ceremony of love and celebration planned by Margarete and inspired in part by George Ezra's song lyric, "You'd better throw a party on the day that I die" ("Green Green Grass"). In characteristic Margarete style, the party featured an aptly named cocktail, "The Last Word," chosen especially by her.

It is little wonder that the many personal tributes following her death have described Margarete as a truly remarkable woman who had a profound impact on the careers and lives of those she encountered and encouraged, remembering not only her intellectual contributions but also her convivial zest for life, her kindness and generosity, her joyful sense of humor, and especially her radiant smile. She is fondly remembered and deeply missed.

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