Prof. Elaine Fuchs
Investigator of the Howard Hughes Medical Institute and Rebecca C. Lancefield Professor of the Rockefeller University

Most important awards, prizes and academies

Academic qualifications: University of Illinois, B.S. Chemistry, 1972, Highest distinction in the curriculum; Princeton University, Ph.D., Biochemistry, 1977; Massachusetts Inst. Technology, Postdoctoral Fellow, 1977-80. *Academies*: American Academy of Arts and Sciences (‘94); National Academy of Medicine (‘94); National Academy of Sciences (‘96); American Philosophical Society (‘05); EMBO Foreign Member (’10); Academy of the American Association for Cancer Research ('13); Academy of the American Society for Cell Biology (’16). *Major Elected Posts in National/International Societies:* President, American Society for Cell Biology, '01; National Academy of Sciences, Council '01-'04; President, Harvey Society, '07; President, International Society for Stem Cell Research (ISSCR), '10; New York Academy of Sciences Board of Governors ('11-); National Academy of Medicine, Council ('14-). *Honours*: University of Illinois 1968-1972: Phi Beta Kappa; Agnes Sloan Larson Award; Iota Sigma Pi Award; Reynold Clayton Fuson Award; James Scholar; Bronze Tablet (top 3% Graduating Class). Massachusetts Institute of Technology 1977-1979: Damon Runyon Postdoctoral Fellow. University of Chicago 1980-2002: Searle Scholar ('81-'83); Presidential Young Investigator Award ('84-'89); Montagna Award (Society for

Investigative Dermatology, '95); Senior Women's Career Achievement Award (American Society for Cell Biology '97); Richard Lounsbery Award (National Academy of Sciences, '01). Rockefeller University. 2002-: Cartwright Prize (Columbia University, '02); Novartis Award in Biomedical Research ('03); Dickson Prize in Medicine ('04); FASEB Award for Scientific Excellence ('06); Beering Award ('06); Lecturer, College de France ('08); National Medal of Science (highest scientific honor in the United States, '09); AACR Charlotte Friend Award ('10); L'Oreal UNESCO Award For Women in Science ('10); Madison Medal (Princeton University '11); Passano Award ('11); Albany Prize in Medicine ('11); March of Dimes Prize in Developmental Biology ('12); Lifetime Achievement Award (American Skin Association '13); Kligman-Frost Leadership Award (Society of Investigative Dermatology '13); Pasarow Award for Cancer Research ('13); Pezcoller International Award for Cancer Research ('14); EB Wilson Award (American Society of Cell Biology '15); Vanderbilt Prize ('17); Ricketts Award (U of Chicago, '17); McEwen Award for Innovation (International Society for Stem Cell Research, '17). *Current Scientific Boards*: Scientific Advisory Board, University of Utah Cancer Center ('12-); Scientific Advisory Board, IMBA Vienna ('12-); Scientific Advisory Board, L'Oreal ('13-); Scientific Advisory Board, Northwestern Skin Center ('15-); Scientific Advisory Board, Sick Kids University of Toronto ('17); Scientific Advisory Board, Massachusetts General Hospital, Harvard Medical School ('17-). *Current Editorial Positions*: Associate Editor, *Journal of Cell Biology*, '93-; Editorial Board, *Genes and Development,* '00-; Editorial Board, *Developmental Cell*, '01-; Editorial Board, *Cell*, '01-; Editorial Board, *Cell Stem Cell*, '07-; Editorial Board *ELife,* '12-.

Summary of scientific research

Each day, over a billion cells in our body die naturally. To replenish dying cells and repair wounds, every tissue of our body has resident stem cells. At the surface of our body, skin is especially vulnerable to physical assaults and pathogens. To cope with these stresses, skin has among the largest reservoirs of adult stem cells. Throughout life, they renew the body's protective barrier, regenerate hair and repair surface wounds. Fuchs studies where stem cells come from and how they make and repair tissues. She explores how stem cells communicate with immune, dermal, and other cells in their environment, and how communication malfunctions in aging and cancers, with an aim to advance therapeutics.

Fuchs' lab couples in vitro studies with classical genetics, RNAi, and CRISPR-Cas gene editing technologies in mice to study the biology of skin stem cells. Her research employs high throughput genomics, single cell sequencing, live imaging, cell biology and functional approaches to unravel the pathways that balance stem cell maintenance and differentiation and to explore aberrant routes in aging and cancers. Her team investigates how stem cells establish unique chromatin landscapes and programs of gene expression, and how this shifts in response to changes in their local environment. They seek to discover the activating signals from neighboring cells that instruct skin stem cells when to make hair and when to repair epidermal injuries. Conversely, inhibitory cross talk tells the stem cells when to stop making tissue and rest. Their findings are accelerating the development of therapeutics to enhance wound repair.

In amassing an understanding of how stem cells become activated at the right time and place to

regenerate tissue, Fuchs' group has begun focusing on what happens when these signals are deregulated. They have uncovered communication pathways between stem cells and local immune cells that are necessary for the skin to efficiently repair damaged skin, but which can pose deleterious consequences in disorders such as psoriasis and atopic dermatitis, where chronic recurrence of inflammation can unleash aberrations in this crosstalk.

The team has also learned that cancer cells hijack the basic mechanisms that enable stem cells to replenish dying cells and to repair wounds. Fuchs' work focuses on squamous cell carcinomas, among the most common and life threatening of human cancers worldwide, affecting not only skin, but also head and neck, esophagus, cervix, lung, breast and thymus. Her laboratory has identified and characterized the so-called "cancer stem cells" that propagate these cancers and which survive chemotherapy, later resurfacing to regrow the cancer. By identifying the mutations that selectively fuel cancer growth, Fuchs hopes her research will lead to therapeutics that target cancer stem cells without affecting tissue stem cells.

Main publications

Adam RC, Yang H, Ge Y, Lien WH, Wang P, Zhao Y, Polak L, Levorse J, Baksh SC, Zheng D, Fuchs E. Temporal Layering of Signaling Effectors Drives Chromatin Remodeling during Hair Follicle Stem Cell Lineage Progression. *Cell Stem Cell* S1934-5909(17)30504-0 (2018); Naik S, Larsen SB, Gomez NC, Alaverdyan K, Sendoel A, Yuan S, Polak L, Kulukian A, Chai S, Fuchs E. Inflammatory memory sensitizes skin epithelial stem cells to tissue damage. *Nature* 550:475-480 (2017). [highlighted in News & Views in *Nature* 550 (2017); Gonzales KAU, Fuchs E. Skin and its regenerative powers: an alliance between stem cells and their niche. *Dev Cel* 43:387-401 (2017); Ge Y, Gomez NC, Adam RC, Nikolova M, Yang H, Verma A, Lu CPJ, Polak L, Yuan S, Elemento O, Fuchs E. Stem cell lineage infidelity drives wound-repair and cancer. *Cell* 169(4):636-650 (2017). [leading edge preview in *Cell* http://dx.doi.org/10.1016/j.cell.2017.04.030]; Yang H, Adam RC, Ge Y, Hua ZL and Fuchs E. Epithelial-mesenchymal micro-niches govern stem cell lineage choices. *Cell* 169(4):636-650 (2017); Asare A, Levorse J and Fuchs E. Coupling organelle inheritance with mitosis to balance growth and differentiation. *Science* 355(6324). pii: eaah4701. doi: 10.1126/science.aah4701. February 3, (2017). PMID:28154022; Sendoel A, Dunn J, Gonzales E, Naik S, Gomez N, Hurwitz B, Levorse J, Dill BD, Schramek D, Molina H, Weissman JS, Fuchs E. Translation from unconventional 5' start sites drives tumor initiation. *Nature* 541(7638):494-499 (2017) PMID: 28077873. [News & Views in *Nature* 541: 471-472 (2017)]; Lu CP, Polak L, Keyes BE and Fuchs E. Spatiotemporal antagonism in mesenchymal-epithelial signaling in sweat versus hair fate decisions. *Science* 354(6319). pii:aah6102. doi: 10.1126/science.aah6102. PMID: 28008008 Dec 23 (2016). [Highlighted in *Science* The "tao" of integuments. Lai YC and Chuong CM 23 Dec 2016: Vol. 354, Issue 6319, pp. 1533-1534]; Keyes BE, Liu S, Asare A, Naik S, Levorse J, Polak L, Lu CP, Nikolova M, Pasolli HA, Fuchs E. Impaired epidermal to dendritic T cell signaling slows wound repair in aged skin. *Cell* 167:1323-1338 (2016); Ouspenskaia T, Matos I, Mertz A, Fiore V, and Fuchs E. WNT-SHH antagonism specifies and expands stem cells prior to niche formation. *Cell* 164:156-69

(2016); Lay K, Kume T and Fuchs E. FOXC1 maintains the hair follicle stem cell niche and governs stem cell quiescence to preserve long-term tissue-regenerating potential. *Proc Natl Acad Sci U S A.* 2016 Feb 24. pii: 201601569. [Epub ahead of print] PMID:26912458; Ge Y, Zhang L, Nikolova M, Reva B, Fuchs E. Strand-specific in vivo screen of cancer-associated miRNAs unveils a role for miR-21* in SCC progression. *Nat Cell Biol.* 18:111-21 (2016); Yang H, Schramek D, Adam RC, Keyes BE, Wang P, Zheng D, Fuchs E. ETS family transcriptional regulators drive chromatin dynamics and malignancy in squamous cell carcinomas. *Elife*. Nov 21; 4, e10870, 1-22 (2015); Oshimori N, Oristian D, Fuchs E. TGF-β promotes heterogeneity and drug resistance in Squamous Cell Carcinoma. *Cell* 160:963-76 (2015); Adam RC, Yang H, Rockowitz S, Larsen SB, Nikolova M, Oristian DS, Polak L, Kadaja M, Asare A, Zheng D., Fuchs E. Pioneer factors govern super-enhancer dynamics in stem cell plasticity and lineage choice. *Nature* 521 366-370 (2015). [*Cell Stem Cell* previews: RJ Whitson & AE Oro, http://dx.doi.org/10.1016/j.stem.2017.01.007]; Blanpain C, Fuchs E. Plasticity of epithelial stem cells in tissue regeneration. *Science* 344:1243-1255 (2014). [cover photo]; Hsu YC, Li L, Fuchs E. Transit-amplifying cells orchestrate stem cell activity and tissue regeneration. *Cell* 157:935-49 (2014); Schramek D, Sendoel A, Segal JP, Beronja S, Heller E, Oristian D, Reva B and Fuchs E. *In vivo* RNAi screen unveils myosin-IIa as a tumor suppressor of Squamous Cell Carcinomas. *Science* 343:309-13(2014); Beronja S, Janki P, Heller E, Lien W-H, Keyes B, Oshimori N, Fuchs E. Genome-wide RNAi screens identify physiological regulators of oncogene-dependent epidermal growth. *Nature* 501:185-90 (2013); Lu CP, Polak L, Rocha AS, Pasolli A, Chen S-C, Sharma N, Blanpain C, Fuchs E. Identification of stem cell populations in sweat glands and ducts: Roles in homeostasis and wound repair. *Cell* 150:136-50 (2012); Hsu YC, Pasolli HA, Fuchs E. Dynamics between stem cells, niche and progeny. *Cell* 144,92-105 (2011). *[highlighted in Cell Stem Cell* 8,8-9, 2011] Fuchs E. The tortoise and the hair: slow-cycling cells in the stem cell race. *Cell* 137,811-819 (2009); Ezhkova E, Pasolli HA, Stokes N, Su I, Tarakhovsky A, Fuchs E. Polycomb protein Ezh2 balances proliferation and differentiation in developing epidermal stem cells. *Cell* 136,1122-1135 (2009); Greco V, Chen T, Rendl M, Schober M, Pasolli HA, Stoke N, de la Cruz-Racelis J, Fuchs E. A two step mechanism for stem cell activation during hair regeneration. *Cell Stem Cell*, 4,155-169 (2009); Yi R, Fuchs E A skin microRNA promotes differentiation by repressing stemness. *Nature* 454, 225-229 (2008); Horsley V., Aliprantis AO, Polak L., Glimcher LH, Fuchs, E. NFTAc1 balances quiescence and proliferation of skin stem cells. *Cell* 132, 299-310 (2008); Lechler T, Fuchs E Asymmetric cell divisions promote stratification and differentiation of mammalian skin. *Nature* 437, 275-280 (2005); Blanpain, C, Lowry W.E, Geoghegan A, Polak, L, Fuchs E. Self renewal, multipotency and the existence of two cell populations within an epithelial stem cell niche. *Cell* 118, 635-648 (2004); Fuchs E, Tumbar T, Guasch G. Socializing with the neighbors: stem cells and their niches. *Cell* 116 769-78 (2004); Tumbar T, Guasch G, Greco V, Blanpain C, Lowry WE, Rendl M, Polak L, Fuchs E. Defining the epithelial stem cell niche of the skin. [Science Express Dec 11, 2003] *Science* 303, 359-363 (2004); DasGupta R, Fuchs E. Distinct roles for activated Lef/Tcf transcription complexes during key steps in hair follicle development and differentiation. *Development*, 126, 4557-4568 (1999); Chan EF, Gat U, McNiff J, Fuchs E. A common human skin tumor is caused by activating mutations in beta-catenin. *Nature Genetics* 21,

410-413, 1999; Gat U, DasGupta R, Degenstein L, Fuchs E. De novo hair follicle morphogenesis and hair tumors in mice expressing a truncated β-catenin in skin. *Cell*, 95, 605-614 (1998); Cleveland DW, Fuchs E. Intermediate filaments in morphogenesis and disease. *Science* 279, 514-19 (1998); Paller AS, Syder AJ, Chan YM, Yu QC, Hutton ME, Hadini G, Fuchs E. Genetic and clinical mosaicism in a type of Epidermal Nevus. *New England Journal of Medicine* 331, 1408-1415 (1994); Cheng J, Syder A, Yu QC, Letai A, Paller AS, Fuchs E. The genetic basis of Epidermolytic Hyperkeratosis: a disorder of differentiation-specific keratin genes. *Cell* 69, 811-819 (1992); Coulombe P, Hutton ME, Letai A, Hebert A, Paller AS, Fuchs E. Point mutations in human K14 genes of Epidermolysis Bullosa Simplex patients: genetic and functional analyses. *Cell* 66, 1301-1311 (1991); Vassar R, Coulombe P, Degenstein L, Albers K, Fuchs E. Mutant keratin expression in transgenic mice causes marked abnormalities resembling a human skin disease. *Cell* 64, 365-380 (1991); Fuchs E, Coppock S, Green H, Cleveland D. Two distinct classes of epidermal keratin genes and their evolutionary significance. *Cell* 27, 75-84 (1981); Fuchs E, Green H. Changes in keratin gene expression during terminal differentiation of the keratinocyte. *Cell* 19, 1033-1042 (1980).

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