Elaine Fuchs

Data di nascita 5 maggio 1950

Luogo Illinois, USA

Nomina 27 marzo 2018

Disciplina Stem cell and cancer biology

Titolo Ricercatrice presso il Howard Hughes Medical Institute e Rebecca C. Lancefield Professor della Rockefeller University

Indirizzo

Howard Hughes Medical Institute

The Rockefeller University

1230 York Avenue, Box 300

New York, NY 10065

USA

Principali premi, riconoscimenti e accademie

Titoli accademici: 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. *Accademie*: 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). *Principali cariche elettive in associazioni nationali/internazionali*: 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-). *Onoreficienze*: 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). *Attuali board scientifici*: 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-). *Attuali cariche editoriali*: 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-.

Riassunto dell'attività scientifica

Ogni giorno nel nostro corpo muoiono di morte naturale oltre un miliardo di cellule. Per ricostituire le cellule morenti e riparare le ferite, in ogni tessuto del nostro corpo risiedono delle cellule staminali. La pelle sulla superficie del nostro corpo è particolarmente vulnerabile agli attacchi fisici e agli agenti patogeni. Per far fronte a questi stress, la pelle è tra i maggiori serbatoi di cellule staminali adulte. Durante tutta la vita, esse rinnovano la barriera protettiva del corpo, rigenerano i capelli e riparano le ferite superficiali. La Dr Fuchs studia la provenienza delle cellule staminali e i loro metodi di produzione e riparazione dei tessuti. Inoltre, esplora come le cellule staminali comunichino nel loro ambiente con le cellule immunitarie, dermiche etc e in che modo si altera questa comunicazione nei processi di invecchiamento e nei tumori, con l'obiettivo di far progredire i metodi terapeutici.

Il laboratorio della Dr Fuchs combina studi in vitro con studi di genetica classica, RNAi e tecnologie CRISPR-Cas di modifica genetica nei topi per studiare la biologia delle cellule staminali della pelle. La sua ricerca utilizza genomica ad alto rendimento, sequenziamento di singole cellule, imaging dal vivo, biologia cellulare e approcci funzionali per svelare i percorsi che bilanciano il mantenimento e la differenziazione delle cellule staminali e per esplorare percorsi aberranti durante l'invecchiamento e nei tumori. Il suo team indaga su come le cellule staminali creino paesaggi di cromatina e programmi di espressione genica unici nel loro genere e su come mutino in risposta a cambiamenti del loro ambiente locale. Inoltre, stanno provando a scoprire quali sono i segnali che attivano le cellule che indicano alle cellule staminali della pelle quando creare capelli e quando riparare le lesioni epidermiche. Il cross talk inibitorio, invece, comunica alle cellule staminali quando smettere di creare tessuti e riposare. Le scoperte del laboratorio della Dr Fuchs stanno accelerando lo sviluppo di terapie per una migliore riparazione delle ferite.

Sulla base di questi studi sull'attivazione delle cellule staminali nel momento e nel luogo giusto per rigenerare il tessuto, il gruppo della Dr Fuchs ha iniziato a concentrarsi su ciò che accade quando questi segnali sono deregolamentati e ha scoperto percorsi di comunicazione tra cellule staminali e cellule immunitarie locali necessari a riparare in modo efficiente la pelle danneggiata. Tuttavia, essi possono avere conseguenze deleterie in disturbi come la psoriasi e la dermatite atopica, dove la recidiva cronica dell'infiammazione può scatenare aberrazioni in questo crosstalk.

Il team ha anche appreso che le cellule tumorali attaccano i meccanismi di base che consentono alle cellule staminali di ricostituire le cellule morenti e di riparare le ferite. Il lavoro della Dr Fuchs si concentra sui carcinomi a cellule squamose, che sono tra i tumori umani più comuni e più mortali a livello mondiale e colpiscono non solo la pelle, ma anche la testa e il collo, l'esofago, la cervice, il polmone, il seno e il timo. Il suo laboratorio ha identificato e caratterizzato le cosiddette "cellule staminali del cancro" che propagano questi tumori e sopravvivono alla chemioterapia, ripresentandosi in seguito per rigenerare il cancro. Identificando le mutazioni che alimentano selettivamente la crescita dei tumori, la Dr Fuchs auspica che la sua ricerca porti a terapie che colpiscano le cellule staminali tumorali senza intaccare le cellule staminali del tessuto.

Pubblicazioni principali

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).

Per una lista completa, consultare

http://www.ncbi.nlm.nih.gov/sites/myncbi/elaine.fuchs.1/bibliography/40603526/public/?sort=date&direction=descending