BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Oro, Anthony Eugene	Professor
eRA COMMONS USER NAME oro.anthony	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Stanford University, Stanford, CA	BS	1985	Biochem, Molecular Bio
University of California, San Diego, La Jolla, CA	PhD	1991	Molecular Genetics
University of California, San Diego, La Jolla, CA	MD	1993	Medicine

A. Personal Statement

I have been studying epithelial biology from the unique perspective of hedgehog signaling since I was a post-doctoral fellow in Matthew Scott's lab in 1995. This unique pathway has provided insights into both human cancer and regenerative medicine, two areas my lab actively investigates. I helped to establish the mechanistic link between the hedgehog pathway and basal cell carcinoma (1997), and establish one of the first human models of skin cancer by using overexpressing hedgehog pathway members in regenerating human epidermis (1997). Using these models we have investigated the basic signaling mechanisms controlling the pathway. These include the role of Gli transcription factor protein degradation (2005), the role of extracellular matrix proteins (2003-2010), and more recently the central role of the primary cilium in controlling spatial and temporal signaling in the hair follicle (2007-2010) and the role of the stroma in epithelial growth(2010). As a practicing Dermatologist, my severe skin cancer patients continue to teach me about the biology of cancer, and encouraged me to find therapeutics that alleviate their suffering. The studies proposed in this grant application thus fall right within my main area of expertise.

B. Positions and Honors

Positions

1998-2006 Assistant Professor, Department of Dermatology, Stanford University, Stanford, CA
2006- Associate member, Stanford Comprehensive Cancer Center
2006-2011 Associate Professor, Department of Dermatology, Stanford University, Stanford, CA
2008- Associate member, Stanford Institute Stem Cell Biology and Regenerative Medicine
2011- Professor, Department of Dermatology, Stanford University, Stanford, CA

Honors:

1981 Academic scholarship, Stanford University
1985 Honors research degree, Stanford University
1985 Fox Award, Stanford University
1987 A. Baird Hastings Honor Society, University of San Diego
1988 Howard Hughes Medical Institute, Graduate Student Award
1996 Thomas Fitzpatrick Research Award, KAO Corporation
1999 Frederick E. Terman Research Award
1999 Charles E. Culpepper Medical Scholar
2006 Nature Publishing Prize, SID Meeting
2008- Stanford Stem Cell Regulatory Board
2010 Permanent Member, ACTS study section

C. Peer-reviewed Publications (40 total)

Fifteen peer-reviewed research papers relevant to this application:

1. Hollenberg, S.M., Weinberger, C., Ong, E.S., Cerelli, G., Oro, A.E, Lebo, R., Thompson, E.B., Rosenfeld, M.G., and Evans R.M. (1985). Primary Structure and Expression of a Functional Human Glucocorticoid Receptor cDNA. **Nature** 318: 635-41. Oro, A.E., McKeown, M., and Evans, R.M. (1990).
2. Oro, A.E., McKeown, M., and Evans, R.M. (1990). Relationship between the product of the Drosophila ultraspiracle locus and the vertebrate retinoic acid responsive transcription factor, the Retinoid X receptor. **Nature** 347: 298-301.
3. Oro, A.E., Higgins, K.M., Hu, Z., Bonifas, J.M., Epstein, E.H., and Scott, M.P. (1997). Basal Cell Carcinomas in Mice Overexpressing Sonic Hedgehog. **Science** 276: 817-21.
4. Fan, H., Oro, A.E., Scott, M.P., and Khavari, P. A. (1997). Induction of basal cell carcinoma features in transgenic human skin expressing Sonic Hedgehog. **Nature Med** 3: 788-92.
5. Aszterbaum, M, ,Epstein, J., Oro, A.E., Douglas, V., LeBoit, P.E., Scott, M.P.,Epstein, E.H. (1999). Ultraviolet and ionizing radiation enhance the growth of BCCs and trichoblastomas in patched heterozygous knockout mice. **Nature Med**. 5: 1285-91.
6. Oro, A.E., Higgins, K. (2003). Hair cycle regulation of Hedgehog signal reception. Dev Bio 255: 238-48.
7. Callahan, C.A., Ofstad, T., Horng L., Wang J.K., Zhen H.H., Coulombe P.A., and Oro A.E. (2004). MIM/BEG4, a Sonic hedgehog-responsive gene that potentiates Gli-dependent transcription. **Genes Dev** 18(22): 2724-9. PMC528890.
8. Gonzalez-Quevedo, R., Shoffer, M., Horng, L., and Oro A. E. (2005). Receptor tyrosine phosphatase-dependent Cytoskeletal remodeling by the hedgehog-responsive gene MIM / BEG4. **J Cell Biol** 168(3): 453-463. PMC2171717.
9. Sarin KY, Cheung P, Gilison D., Lee E, Tennen R.I., Wang E., Artandi M.K., Oro A.E., Artandi S.E. (2005). Conditional telomerase induction causes proliferation of hair follicle stem cells. **Nature** 436(7053): 1048-52. PMC1361120.
10. Huntzicker E.G., Estay I, Zhen H., Lokteva L.A., Jackson P. K., Oro A.E. (2006). Dual degradation signals control Gli stability and tumor formation. **Genes Dev** 20: 276-81. PMC1361699.
11. Sneddon, J.B., Zhen, H.H., Montgomery, K., van de Rijn, M., Tward, A.D., West, R., Gladstone, H., Chang, H., Morganroth, G.S., Oro, A.E., Brown. P.O. (2006). BMP Antagonist Gremlin 1 is Widely Expressed by Cancer-associated Stromal Cells and Can Promote Tumor Cell Proliferation. **Proc Natl Acad Sci USA** 103: 14842-7. PMC1578503.
12. Gao, J., DeRouen, M., Chen, C-H., Nguyen, M., Nguyen, N.T., Ido, H., Harada, K., Sekiguchi, K., Morgan, B.A., Miner, J., Oro, A.E. and Marinkovich, M.P. (2008). Laminin-511 is an epithelial message promoting dermal papilla development and function during early hair morphogenesis. **Genes Dev**, Aug 1;22(15):2111-24.
13. Quinones GA, Jin J, Oro AE. I-BAR protein antagonism of endocytosis mediates directional sensing during guided cell migration. ***J Cell Biol***. 2010 Apr 19;189(2):353-67.
14. Bershteyn M, Atwood SX, Woo W-M, Li M, Oro AE. MIM and cortactin antagonism regulates ciliogenesis and Hedgehog signaling. ***Dev Cell.*** 2010 Aug 17;19(2):270-283.
15. DeRouen, MC, Zhen, H., Tan, SH, Williams, S, Marinkovich, MP, and Oro, AE, Laminin-511 and Integrin beta-1 in hair follicle development and basal cell carcinoma formation 2010 **BMC Dev Biol** 10:112.

Five peer-reviewed "review articles" relevant to this grant application:

1. Oro, A.E. and Scott, M.P. (1998). Splitting Hairs: Dissecting Roles of Signaling Systems in Epidermal Development, **Cell** 95: 575-578.
2. Huntzicker E.G., Oro, A.E. (2008). Controlling Hair Follicle Signaling Pathways through Polyubiquitination. **J Invest Dermatol** 128: 1081-7.
3. Oro A.E. (2007). The Primary cilia, a 'Rab-id' transit system for hedgehog signaling. **Curr Opin Cell Biol** 19: 691-6.
4. DeRouen MC, Oro AE. The primary cilium: a small yet mighty organelle. ***J Invest Dermatol.*** 2009 Feb;129(2):264-5. Review.
5. Woo, W-M, and Oro AE. SnapShot: Hair Follicle Stem Cells. ***Cell***, 2011, in press.

D. RESEARCH SUPPORT

On Going Support

R01 AR46786 (Anthony E. Oro, PI) 09/25/06 - 08/31/11
NIH
Stromal Regulation of Basal Cell Carcinoma Formation
The major goal of this project is to understand the molecular basis of epithelial regulation of Shh signaling. We have found that polarity protein controls cellular responsiveness as does several non-cell autonomous stromal proteins.
Current Proposal

R01 AR054780 (Anthony E. Oro, PI) 05/07/07 - 02/28/12
NIH
Regulating Gli Function in Hair Follicle Progenitors
The major goal of this project is to understand the regulation of hair follicle epithelial stem cell signaling. We have been focusing on the timing of the anagen/telogen onset.
Overlap: None

R01 AR052785 (Anthony E. Oro, PI) 06/01/07 – 05/31/12
NIH
BEG4/MIM Function in Epithelial Neoplasia
The major goal of this project is to understand how the BAR domain-containing MIM protein functions in Shh-dependent signaling and cellular invasion using Drosophila and mouse genetics.
Overlap: None

California Institute for Regenerative Medicine (Anthony E. Oro, Co-PI) 05/1/10-04/30/14
iPS cell Based Therapy for Dystrophic EB
The major goal of this project is to develop a detailed understanding and protocol to produce patient-specific epithelial sheets carrying genetically-corrected keratinocytes from induced pleuripotent cells.
Overlap: None

California Institute for Regenerative Medicine (Michaeal Longaker, PI) 9/1/09-8/31/11
Wnt functions in Regenerative Medicine
The goal of this project is to assay the therapeutic potential of Wnt liposomes in skin, bone, brain, and heart.
Overlap: None

SHH4476G (Oro) 11/17/08-05/01/11
Genentech, Inc.
A Pivotal, phase II, multicenter, single-arm, two-cohort trial evaluating the short term efficacy and safety of GDC-0449 in patients with advanced basal cell carcinoma.
Overlap: None

SHH4437G (Oro) 09/11/09-07/31/11
Genentech, Inc.
A single-arm trial evaluating the efficacy and safety of GDC-0449 in patients with advanced basal cell carcinoma.
Overlap: None

SHH4811G (Oro) 07/23/10-04/01/12
Genentech, Inc.
Multicenter, single-arm, trial evaluating the long term efficacy and safety of GDC-0449 in patients with advanced basal cell carcinoma.
Overlap: None

IPI-926-01 (Oro) 03/09/10-02/29/12
Infinity Pharmaceuticals
A phase I, multicenter, single-arm, trial evaluating the efficacy and safety of IPI-926 in patients with advanced basal cell carcinoma.
Overlap: None