PAULA JEAN KAPLAN-LEFKO, Ph.D.

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MEDICAL/REGULATORY WRITER; PROJECT MANAGER

- Wrote and submitted investigational new drug (IND) application to Food and Drug Administration (FDA) for investigator-initiated oncology adoptive cell transfer (ACT) gene therapy clinical trial
- Wrote and coordinated review of pre-IND application for gene therapy clinical trial using stem cells, submitted document and facilitated meeting to obtain FDA guidance
- Managing project leading to an investigator-initiated trial funded by a $20M grant including regulatory oversight, managing timelines and regulatory writing
- Wrote and coordinated review of 5 clinical protocols and informed consent forms (ICF)
- Wrote pharmacology section of 2 IND applications and investigator brochures (IB) leading to successful first-in-human (FIH) drug administration at biotech company
- Wrote and was awarded 3 grants providing funding for postdoctoral laboratory
- Drove authoring, review and approval of manuscripts and study reports through validated electronic data management system; Consistently achieved timelines; Managed team to achieve consensus
- Effective communicator with exceptional writing skills; known as excellent collaborator and strong team player; Proficient using Microsoft Word, Powerpoint and Excel
- One and a half years experience managing investigator-initiated clinical trials in oncology including regulatory writing/coordination and project management
- Nine years oncology research experience at a biotech company with expertise in *in vivo* pharmacology

PROFESSIONAL EXPERIENCE

UNIVERSITY OF CALIFORNIA, LOS ANGELES (UCLA), CA 2012 - present
Regulatory Coordinator/Regulatory Writer/Project Manager

- Wrote, coordinated review and submitted IND and pre-IND documents to the FDA for investigator-initiated clinical trials; Participated in FDA audit of gene therapy trial

UCLA (continued)

- Wrote 3 clinical protocols and ICFs and submitted to the UCLA Institutional Review Board (IRB) for eventual submission to the FDA; Wrote 1 tissue/blood banking and 1 screening protocol and ICF
- Managing regulatory oversight for investigator-initiated trials ensuring approvals from all required UCLA committees and federal agencies
- Project manager responsible for all regulatory activities for proposed clinical trial, coordinating information to the granting agency, coordinating meetings and activities of the investigators to ensure that milestones are met to enable clinical trial to begin in a timely manner
- Drove authoring, review and submission of a multi-investigator NIH equipment grant
- Wrote preclinical toxicology protocols, coordinated review of protocols, facilitated meeting with the FDA to review protocols, managing the establishment of Good Laboratory Practice (GLP) procedures to enable toxicology studies, coordinating writing of SOPs
- Wrote animal protocols and coordinated approval of animal protocols by the institutional animal research committee

AMGEN, INC., Thousand Oaks, CA 2002 - 2011
Oncology Research
Principal Scientist, 2009 - 2011
Senior Scientist, 2005 - 2009
Research Scientist I, 2002 - 2005

Developed small molecule and protein therapeutics for oncology indications; pharmacology representative on multiple teams; projects ranged from early discovery to phase 2; Lead author on 1 manuscript; Contributing author on 10 manuscripts

- Led pharmacology effort on multiple teams leading to successful FIH drug administration
- Wrote/edited pharmacology section of IND applications and IBs, manuscripts, posters, annual reports and study reports
- Supervised research associates performing *in vivo* pharmacology experiments to evaluate efficacy and mechanism of action of compounds, to evaluate potential biomarkers, to assess pharmacokinetic/pharmacodynamic (PK/PD) relationship and to rank order compounds *in vivo*; Utilized xenograft models, transgenic models and PD models

POSTDOCTORAL TRAINING

Baylor College of Medicine, Houston, TX 1996 - 2002
Department of Molecular and Cellular Biology
Postdoc Advisor: Dr. Norman M. Greenberg

- Examined the role of the insulin-like growth factor (IGF) axis in the genesis and progression of metastatic prostate cancer using transgenic animal models
- Wrote 5 grants and wrote/edited multiple manuscripts and posters
- Lead author on 3 manuscripts; Contributing author on 7 manuscripts

EDUCATION

Ph.D. in Biology 1989 - 1996
Tufts University, Department of Biology, Medford, MA
Thesis advisor: Dr. Shuk-Mei Ho. Thesis title: Involvement of the Epidermal Growth Factor family and steroid hormones in normal and aberrant prostatic growth.

- Lead author on 1 manuscript; Contributing author on 1 manuscript

B.A. in Biology 1983 - 1988
Scripps College, Joint Science Department, Claremont, CA
Thesis advisor: Dr. Alan Jones. Senior thesis title: The effects of gestational undernutrition and caffeine exposure on body weight.

Study Abroad, Hebrew University, Jerusalem, Israel 1985 - 1986

GRANTS AWARDED

National Institutes of Health, Biochemical Endocrinology Study Section, R01, "IGF Axis in Prostate Cancer: A Transgenic Study", Co-authored with postdoc advisor, Norman Greenberg (1999-2004)

Association for the Cure of Cancer of the Prostate (CaP CURE), Young Investigator Award, "Abrogation of IGF1R as Therapy for Prostate Cancer", Principle Investigator (2000-2003)

National Cancer Institute, National Research Service Award, "IGF in Prostate Cancer: A Transgenic Study", Principle Investigator (1997-2000)

TEACHING EXPERIENCE

University of California at Santa Barbara
- Guest lecturer for Pharmacology class on "The Use of Preclinical Models in Drug Development"

The Jackson Laboratory, Bar Harbor, ME
- Teaching Assistant at the Techniques for Modeling Human Cancer in Mice Workshop

Tufts University, Department of Biology, Medford, MA
- Teaching assistant in Endocrinology, Microbiology, Genetics, Experiments in Biology and Introductory Biology
- Howard Hughes Foundation Teaching Scholar Program participant. Prepared and presented lectures in Endocrinology.

PATENTS

Teresa Burgess, Angela Coxon, Isabelle Dussault, **Paula Kaplan-Lefko**, Anthony Polverino and Darrin Beaupre. Combinations VEGF (R) Inhibitors and Hepatocyte Growth Factor (c-Met) Inhibitors for the Treatment of Cancer. *US 2011/0104161 A1*; May 5, 2011.

PROFESSIONAL MEMBERSHIP

Member of the American Medical Writers Association (2011 - present); AMWA certification expected completion 2014 (2011 - present)
Member of the American Association for Cancer Research (1992 – present)

PUBLICATIONS

Payton M, Jun T, Wayne W, Yu D, Manoukian R, Chung G, Zhang N, Sun, J-R, **Kaplan-Lefko P,** Radinsky R, Kendall R, Oliner J, and Coxon A. 2013. Antagonism of angiopoietin-Tie2 and Dll4-Notch signaling mediate distinct and opposing effects on tumor xenograft-associated mouse endothelial cell proliferation, as evidence by a new multiparametric flow cytometry method. *Laboratory Investigation,* in preparation.

Rossin R, Kohno T, Hagooly A, Sharp T, Gliniak B, Arroll T, Chen Q, Hewig A, **Kaplan-Lefko P**, Friberg G, Radinsky R, Evelhoch JL, Welch MJ, Hwang DR. 2011. Characterization of 64Cu-DOTA-conatumumab: a PET tracer for in vivo imaging of death receptor 5. *J Nucl Med.* 52:942-9.

Kaplan-Lefko PJ, Graves JD, Zoog SJ, Pan Y, Wall J, Branstetter DG, Moriguchi J, Coxon A, Huard JN, Xu R, Peach ML, Juan G, Kaufman S, Chen Q, Bianchi A, Kordich JJ, Ma M, Foltz IN and Gliniak BC. 2010. Conatumumab, a fully human agonist antibody to death receptor 5, induces apoptosis via caspase activation in multiple tumor types. *Cancer Biol Ther.* 9:618-31.

Zoog SJ, Ma CY, **Kaplan-Lefko PJ**, Hawkins JM, Moriguchi J, Zhou L, Pan Y, Hsu CP, Friberg G, Herbst R, Hill J and Juan G. 2010. Measurement of conatumumab-induced apoptotic activity in tumors by fine needle aspirate sampling. *Cytometry A.* 77:849-60.

Gordon MS, Sweeney CS, Mendelson DS, Eckhardt SG, Anderson A, Beaupre DM, Branstetter D, Burgess TL, Coxon A, Deng H, **Kaplan-Lefko P**, Leitch IM, Oliner KS, Yan L, Zhu M and Gore L. Safety, pharmacokinetics, and pharmacodynamics of AMG 102, a fully human hepatocyte growth factor-neutralizing monoclonal antibody, in a first-in-human study of patients with advanced solid tumors. 2010. *Clin Cancer Res.* 16:699-710.

Boezio AA, Berry L, Albrecht BK, Bauer D, Bellon SF, Bode C, Chen A, Choquette D, Dussault I, Fang M, Hirai S, **Kaplan-Lefko P**, Larrow JF, Lin MH, Lohman J, Potashman MH, Qu Y, Rex K, Santostefano M, Shah K, Shimanovich R, Springer SK, Teffera Y, Yang Y, Zhang Y, Harmange JC. 2009. Discovery and optimization of potent and selective triazolopyridazine series of c-Met inhibitors. *Bioorg Med Chem Lett.* 19:6307-12.

D'Angelo ND, Bellon SF, Booker SK, Cheng Y, Coxon A, Dominguez C, Fellows I, Hoffman D, Hungate R, **Kaplan-Lefko P**, Lee MR, Li C, Liu L, Rainbeau E, Reider PJ, Rex K, Siegmund A, Sun Y, Tasker AS, Xi N, Xu S, Yang Y, Zhang Y, Burgess TL, Dussault I and Kim TS. 2008. Design, synthesis, and biological evaluation of potent c-Met inhibitors. *J. Med. Chem.* 51:5766-5779.

Zhang Y, **Kaplan-Lefko PJ**, Rex K, Yang Y, Moriguchi J, Osgood T, Mattson B, Coxon A, Reese M, Kim TS, Lin J, Chen A, Burgess TL and Dussault I. 2008. Identification of a novel recepteur d'origine nantais/c-Met small-molecule kinase inhibitor with antitumor activity in vivo. *Cancer Res.* 68:6680-6687.

Liu L, Siegmund A, Xi N**, Kaplan-Lefko P**, Rex K, Chen A, Lin J, Moriguchi J, Berry L, Huang L, Teffera Y, Yang Y, Zhang Y, Bellon SF, Lee M, Shimanovich R, Bak A, Dominguez C, Norman MH, Harmange JC, Dussault I and Kim TS. 2008. Discovery of a potent, selective, and orally bioavailable c-Met inhibitor: AMG 458. *J Med Chem.* 51:3688-91.

Sutherland BW, Knoblaugh SE, **Kaplan-Lefko PJ**, Wang F, Holzenberger M and Greenberg NM. 2008. Conditional deletion of IGF1R in prostate epithelium. *Cancer Res.* 68:3495-3504.

Albrecht BK, Harmange JC, Bauer D, Berry L, Bode C, Boezio AA, Chen A, Choquette D, Dussault I, Fridrich C, Hirai S, Hoffman D, Larrow JF, **Kaplan-Lefko P**, Lin J, Lohman J, Long AM, Moriguchi J, O'Connor A, Potashman MH, Reese M, Rex K, Siegmund A, Shah K, Shimanovich R, Springer SK, Teffera Y, Yang Y, Zhang Y and Bellon SF. 2008. Discovery and optimization of triazolopyridazines as potent and selective inhibitors of the c-Met kinase. *J Med Chem.* 51:2879-82.

Bellon SF, **Kaplan-Lefko P**, Yang Y, Zhang Y, Moriguchi J, Rex K, Johnson CW, Rose PE, Long AM, O'Connor AB, Gu Y, Coxon A, Kim TS, Tasker A, Burgess TL, Dussault I. 2008. c-Met inhibitors with novel binding mode show activity against several hereditary papillary renal cell carcinoma-related mutations. *J Biol Chem.* 283:2675-83.

Jun HT, Stevens J and **Kaplan-Lefko P**. 2008. Top NOTCH Targets: Notch Signaling in Cancer (Review). *Drug Development Research.* 69:319-328.

Kaplan-Lefko PJ, Sutherland BW, Evangelou AI, Hadsell DL, Barrios RJ, Foster BA, DeMayo F and Greenberg NM. 2008. Enforced epithelial expression of IGF-1 causes hyperplastic prostate growth while negative selection is requisite for spontaneous metastogenesis. *Oncogene.* 27:2868-76.

Morgenbesser SD, McLaren RP, Richards B, Zhang M, Akmaev VR, Winter SF, Mineva ND, **Kaplan-Lefko PJ**, Foster BA, Cook BP, Dufault MR, Cao X, Wang CJ, Teicher BA, Klinger KW, Greenberg NM, Madden SL. 2007. Identification of genes potentially involved in the acquisition of androgen-independent and metastatic tumor growth in an autochthonous genetically engineered mouse prostate cancer model. *Prostate.* 67:83-106.

Majeed N, Blouin MJ, **Kaplan-Lefko PJ**, Barry-Shaw J, Greenberg NM, Gaudreau P, Bismar TA, Pollak M. 2005. A germ line mutation that delays prostate cancer progression and prolongs survival in a murine prostate cancer model. *Oncogene.* 24:4736-40.

Kaplan-Lefko, PJ, Chen, TM, Maddison, LA, Huss, WJ, Barrios, R, Ittman, M, Ayala, G and Greenberg, NM. 2003. Pathobiology of autochthonous prostate cancer in a transgenic mouse model. *Prostate.* 55(3):219-237.

Uzgare, AR, **Kaplan, PJ** and Greenberg, NM. 2003. Differential expression and activation of p38 MAPK, Erk 1/2 and Jnk during the initiation and progression of prostate cancer. *Prostate.* 55(2):128-139.

Foster, BA, Evangelou, A, Gingrich, JR, **Kaplan, PJ**, DeMayo, F and Greenberg, NM. 2002. Enforced expression of FGF-7 promotes epithelial hyperplasia whereas a dominant negative FGFR2iiib promotes the emergence of neuroendocrine phenotype in prostate glands of transgenic mice. *Differentiation.* 70(9-10):624-632.

Kaplan, PJ, Mohan, S, Cohen, P, Foster, BA and Greenberg, NM. 1999. The IGF axis and prostate cancer: Lessons from TRAMP. *Cancer Research.* 59:2203-2209.

Foster, BA, **Kaplan, PJ** and Greenberg, NM. 1999. Peptide growth factors and prostate cancer: New models, new opportunities. *Cancer and Metastasis Reviews.* 17:317-324.

Foster, BA, **Kaplan, PJ** and Greenberg, NM. 1999. Characterization of the FGF axis and identification of a novel FGFR1iiic isoform during prostate cancer progression in the TRAMP model. *Prostate Cancer and Prostatic Diseases.* 2:76-82.

Kaplan, PJ, Leav, I, Greenwood, J, Kwon, PWL and Ho, S-M. 1996. Involvement of transforming growth factor α (TGFα) and epidermal growth factor receptor (EGF_R) in sex hormone-induced prostatic dysplasia and the growth of an androgen-independent transplantable carcinoma of the prostate. *Carcinogenesis.* 17:2571-2579.

Ghatak, S, Oliveria, P, **Kaplan, P** and Ho, S-M. 1996. Expression and regulation of metallothionein mRNA levels in the prostates of Noble rats: Lack of expression in the ventral prostate and regulation by sex hormones in the dorsolateral prostate. *The Prostate.* 29:91-100.

SELECTED POSTERS AND ORAL PRESENTATIONS

Kaplan-Lefko P*, Rex K*, Zhang Y, Yang Y, Kha H, Ziegler B, Moriguchi J, Mallari M, Zhao X, Choquette D, Lewis, R Lin J, Shimanovich R, Broome M and Dussault I. In Vitro and In Vivo Profiling of Class I and Class II ATP-Competitive c-Met Kinase Inhibitors Defines Potential c-Met-Specific Sensitivity Biomarkers. *AACR Annual Meeting*, 2011. *Contributed equally (poster)

Kaplan-Lefko P, Bush T, Belmontes B, Moriguchi J, Dansey M, Osgood T, Canon J, Van Der Vuurst De Vries A-R, Graves J, Branstetter D, Coxon A and Gliniak B. AMG 655, a fully human agonist antibody against death receptor 5, enhances the anti-tumor activity of gemcitabine in MiaPaCa2/T2, a pancreatic cancer model. *AACR Annual Meeting*, 2008 (poster)

Kaplan-Lefko P, Rex K, Moriguchi J, Yang Y, Zhang Y, Chen A, Lin J, Kaufman S, Kim T-S, Liu L, Siegmund A, Harmange JC, Shimanovich R, Burgess T, Kendall R, Radinsky R,

Coxon A and Dussault I. AMG 458, a potent small molecule c- Met inhibitor, has significant anti-tumor activity in vivo. *AACR Annual Meeting*, 2008 **(oral presentation)**

Kaplan-Lefko, PJ. Animal Model Selection for Efficacy with Biologics for Cancer. *Biosafe General Membership Meeting,* 2007 **(oral presentation)**.

Kaplan-Lefko P, Gan Y, Huard J, Colloton M, Zoog S, Juan G, Dobson T, Peach M, Pan Y, Kaufman S, Branstetter D, Coxon A, Bianchi A, Wong-Madden S, Foltz I and Gliniak B. AMG 655, a fully human agonistic antibody against TRAIL receptor-2, induces apoptosis via caspase activation in vitro and in vivo. *American Association for Cancer Research Annual Meeting*, 2007 (poster).