BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Koeffler, H. Phillip	Professor of Medicine
eRA COMMONS USER NAME (credential, e.g., agency login) koefflerp	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Wisconsin, Madison, WI	BA	06/1968	Zoology
Baylor College of Medicine	MD	06/1972	Medicine
USC Medical Center, Los Angeles, CA	Internship	1975	Medicine
UCLA School of Medicine, Los Angeles, CA	Fellowship	1978	Hem/Onc

A. Personal Statement

I am a Professor of Medicine at UCLA School of Medicine (Cedars-Sinai Medical Center) and holder of the Mark Goodson Chair in Oncology Research at Cedars-Sinai Medical Center. I have over 745 peer-reviewed scientific articles, most dealing with normal and malignant hematopoiesis. I have mentored about 200 post-docs and a similar number of students during my career. Most of the post-docs have continued in academic careers and many of the students have entered professional schools.

B. Positions and Honors

6/78 - 8/78	Visiting Scientist, University of Chicago, Department of Biochemistry, (Eugene Goldwasser, Ph.D.)
6/78 - 7/82	Assistant Professor of Medicine, UCLA, Division of Hematology/Oncology, Department of Medicine, Los Angeles, California
7/79 - 9/79	Visiting Scientist, Department of Molecular Biology, California Institute of Technology, Pasadena, California, (Dr. Thomas Maniatis)
7/82 - 7/86	Associate Professor of Medicine, Division of Hematology/Oncology, University of California, Los Angeles, Los Angeles, California
7/86 - Present	Professor of Medicine, Division of Hematology/Oncology, University of California, Los Angeles, Los Angeles, California
4/90 – 7/10	Director, Division of Hematology/Oncology, Cedars-Sinai Medical Center, Professor of Medicine, UCLA School of Medicine, Los Angeles, CA
1/97 - Present	Holder of The Mark Goodson Chair in Oncology Research, Cedars-Sinai Medical Center
2008 - Present	Professor of Bioengineering, University of California Los Angeles, Los Angeles, CA
2009 – Present	Professor of Medicine, Yong Loo Lin School of Medicine, National University of Singapore
2009 – Present	Senior Principal Investigator, Cancer Science Institute of Singapore, National University of Singapore
1/14 – present	Adjunct Clinical Professor of Medicine, Keck School of Medicine, USC, Los Angeles, CA

National Society of Clinical Investigation	1978 – To Present
Scholar, Leukemia Lymphoma Society	1978 – 1983
Holder of the Mark Goodson Chair in Oncology Research (CSMC)	1997 – to present
American Association of Physicians	2013 – to present

C. Contribution to Science:

- **Koeffler HP**, Golde DW. Acute myelogenous leukemia: a human cell line responsive to colony-stimulating activity. **Science**, 200:1153-1154, 1978
- Munker R, Gasson J, Owaga M and **Koeffler HP**. Recombinant human tumor necrosis factor induces production of granulocyte-monocyte colony stimulating factor. **Nature**, 323:79, 1986

Since the beginning of my career, one focus has been normal and aberrant hematopoiesis with particularly emphasis on leukemia. Early accomplishments included my development of the KG1 acute myelogenous leukemia (AML) cell line, an understanding of the importance of cytokines and hematopoiesis.

- Reichel H, **Koeffler HP**, Norman AW. The role of the vitamin D endocrine system in health and disease. **N Engl J Med**. 320:980-991, 1989

I also focused on understanding of the vitamin D pathway in normal and abnormal hematopoiesis in cancer and was first to prove that activated macrophages was a source 125-dihydroxy vitamin D3.

- Masuda H, Miller C, **Koeffler HP**, Battifora H, Cline MJ. Rearrangement of the p53 gene in human osteogenic sarcoma. **Proc Natl Acad Sci USA**, 84:7716-7719, 1987.
- O'Rourke RW, Miller CW, Kato GJ, Simon KJ, Chen DL, Dang CV and **Koeffler HP**. A potential transcriptional activation element in the p53 protein. **Oncogene**, 1829-1832, 1990

We were the first to discover p53 alterations in human cancers, and were one of several labs to define p53 as a transcription factor.

- Chumakov AM, Grillier I, Chumakova E, Chih D, Slater J and **Koeffler HP**. Cloning of the Novel Human Myeloid-Cell-Specific C/EBPε- Transcription Factor. **Mol. Cell. Biol.**, 17(3) 1375-1386, 1997
- Kyme P, Thoennissen NH, Tseng C-W, Thoennissen G, Wolf A, Shimada K, Krug U, Lee K, Muller-Tidow C, Berdel WE, Hardy WD, Gombart A, ***Koeffler HP** and *Liu G. C/EBPepsilon mediates nicotinamide-enhanced clearance of Staphylococcus aureus in mice. , **J Clin Invest**, 122(9): 3316-29, 2012

As molecular techniques evolved, we were one of two labs to clone the myeloid specific transcription factor, CEBPε and did numerous studies of its normal and aberrant regulation.

Most recently, we showed that stimulation of C/EBPε is a mechanism to enhance antimicrobial activity.

- Kawabata H, Yang R, Hirama T, Vuong P, Kawano S, Gombart A and **Koeffler HP**. Molecular Cloning of Transferrin Receptor 2 (TfR2): A New Member of the Transferrin Receptor-like Family. **J Biol Chem** 274(30):20826-32, 1999

We were first to clone transferrin receptor 2 and we continue to do studies on iron metabolism.

- Müller C, Yang R, Beck-von-Peccoz L, Idos G, Verbeek W and **Koeffler HP**. Cloning of the *cyclin A1* Genomic Structure and Characterization of the Promoter Region. GC boxes are essential for cell cycle regulated transcription of the cyclin A1 gene. **J Biol Chem**, 274(16):11220-8, 1999

We were first to clone human cyclin A1 and do subsequent biological studies.

- Kawamata N, Ogawa S, ….Bartram C, **Koeffler HP**. Cloning of genes involved in chromosomal translocations by high resolution single nucleotide polymprphism genomic microarray. **Proc. Natl Acad Sci**. 105(33):11921-6, 2008
- Kawamata N, Pennella MA, Woo JL, Berk AJ, **Koeffler HP**. Dominant-negative mechanism of leukemogenic PAX5 fusions. **Oncogene** 31(8):966-77, 2012)

We have been studying the molecular landscape of various cancers including AML, initially using SNP-ChIP arrays. These studies led to the observation that many fusion genes contained a DNA binding sequence from one partner gene and a multimerization sequence from the other partner allowing the fusion product to behave in a dominant negative fashion. We evolved this observation by constructing and testing a universal dominant negative peptide consisting of the DNA binding motif of an oncogenic transcription factor fused to the p53 tetramerization sequence.

- Yoshida K, Sanada M, Shiraishi Y, Nowak D, Nagata Y Yamamoto R, Sato Y, Sato-Otsubo A, Kon A, Nagasaki M, Chalkidis G, Suzuki Y, Shiosaka M, Kawamata R, Yamaguchi T, Otsu M, Obara N, Sakata-Yangimoto M, Ishiyama K, Mori H, Nolte F, Hofmann WK, Miyawaki S, Sugano S, Haferlach C, **Koeffler HP**, Shih LY, Haferlach T, Chiba S, Nakauchi H, Miyano S, Ogawa S. Frequent pathway mutations of splicing machinery in myelodysplasia. **Nature**. 478(7367):64-9, 2011
- Madan V, Kanojia D, Li J, Okamoto R, Sato-Otsubo A, Kohlmann A, Sanada M, Grossmann V, Sundaresan J, Shiraishi Y, Miyano S, Thol F, Ganser A, Yang H, Haferlach T, Ogawa S and Koeffler HP. Aberrant splicing of U12-type introns is the hallmark of ZRSR2 mutant myeloysplastic syndrome. Nat Commun 2015, Jan 14:6:6042. PMID: 25586593

We have been using high throughput sequencing to analyze a variety of cancers including MDS where we identified mutations of the spliceosome genes. In particular, we are studying mutant ZRSR-2 and its missplicing.

- Lin D, Meng X, Hazawa M, Nagata Y, Varela AM, Xu L, Sata Y, Liu LZ, Sing LW, Sharma A, Goh BC, Lee SC, Petersson BF, Yu FG, Macary P, Oo MZ, Ha CS, Yang H, Ogawa S, Loh KS,.Koeffler HP. The genomic landscape of nasopharyngeal carcinoma. Nature Genetics. 46(8):866-71, 2014 PMID 24952746.
- Lin DC, Hao JJ, Nagata Y, Xu L, Shang L, Meng X, Sata Y, Okuno Y, Varela AM, ding LW, Garg M, Liu LZ, Yang H, Yin D, Shi ZZ, Jiang YY, Gu WY, Gong T, Zhang Y, Xu X, Kalid O, Shacham S, Ogawa S, Wang MR, Koeffler HP. Genomic and molecular characterization of esophageal squamous cell carcinoma. Nat Genet. 46(5):467-73, 2014 PMID: 24686850

We have been studying the genomic changes in esophageal and nasopharyngeal cancers.