MOHAMMED TAIMI, Ph.D.

From northern Moroccan city of Ksar-El-Kebir. He received his undergraduate and Ph.D degrees in Biochemistry from universities of Aix-Marseille and Montpellier, France. He spent over 5 years as postdoc fellow at the National Cancer Institute, NIH, working on acquire drug resistance in cancer due to drug metabolism. He joined the pharmaceutical industry, first in a small Biotech company in Ontario/Canada as Senior Scientist and Project Leader of the drug metabolism group. Currently, he is Associate Director of the drug metabolism and pharmacokinetic group (DMPK) at Synta Pharmaceuticals in the Boston area, with main focus on discovery and development of inflammation and cancer drugs

KEY PROFESSIONAL ACCOMPLISHMENTS

Utilized experience in quantitative bioanalysis, drug metabolism, pharmacokinetics and metabolite identification to make positive impacts on drug discovery and development with extensive expertise in:

- Advance bioanalytical technologies, LC/MS/MS
- ADME/PK screening strategy to support development of novel drug candidates from early discovery, lead-optimization, preclinical development
- *in vitro* and *in vivo* assays to assess drug exposure and investigate issues related to ADME/PK
- Qualitative bioanalytical analysis for metabolite Identification studies in various species both in vitro and in vivo (human, relevant species), with critical feedback to both medicinal chemistry group to design drugs with improved properties, and to toxicology group for selecting appropriate species for preclinical toxicology studies
- Reactive metabolite evaluation at early stage of discovery and establish risk-mitigation associated with human idiosyncratic adverse reactions
- PK data analysis and interpretation: rodent PK (noncompartmental), TK, dose-dependency PK, excretion studies, and tissue distribution
- Non-rodent PK studies (dog, monkey): evaluate exposure level, clearance, therapeutic index,..etc

- First-in human dose projection: interspecies allometic scaling, PK simulation, PK/PD, PBPK (WinNonLin, GastroPlus)
- Championed in ADME/PK nomination criteria in early discovery stage (first-in-class vs. best-in-class) in a multidisciplinary drug discovery team including chemistry, pharmacology and toxicology groups

Active member of American Association of Pharmaceutical Sciences (AAPS), International Society for the Study of Xenobiotics (ISSX) and American Association of Cancer Research (AACR)

PUBLICATIONS

1. Parise R. A., Egorin M. J., Kanterewicz B., **Taimi M**., Petkovich M., Lew A. M., Chuang S. S., Nichols M., El-Hefnawy T., and P. A. Hershberger. **2006**. CYP24, the enzyme that catabolizes the antiproliferative agent vitamin D, is increased in lung cancer. *International Journal of Cancer* 119 (8):1819-28.

2. **Taimi M.,** Helvig C., Wisniewski J., Ramshaw H., White J., Amad M., Korczak B. and Petkovich M. **2004**. A novel human cytochrome P450, CYP26C1, involved in metabolism of 9-cis and all-transisomers of retinoic acid. *J. Biol. Chem.* 279 (1):77-85.

3. Chuang SS., Helvig C., **Taimi M.,** Ramshaw HA., Collop AH., Amad M., White JA., Petkovich M., Jones G., and Korczak B. **2004**. CYP2U1, a novel human thymus- and brain-specific cytochrome P450, catalyzes omega- and (omega-1)-hydroxylation of fatty acids. *J. Biol. Chem.* 279 (8):6305-14.
4. **Taimi M,** Breitman TR and Takahashi N**. 2001**. Cyclic AMP-dependent protein kinase isoenzymes in human myeloid leukemia (HL60) and breast tumor (MCF-7) cells. *Arch Biochem Biophys*.392 (1):137-44.

5. White JA., Ramshaw H., **Taimi M.**, Stangle W., Zhang A., Everingham S., Creighton S., Tam SP., Jones G. and Petkovich M. **2000**. Identification of the human cytochrome P450, P450RAI-2, which is predominantly expressed in the adult cerebellum and is responsible for all-trans-retinoic acid metabolism. *Proc Natl. Acad. Sci. U S A*. 97 (12):6403-8.

6. **Taimi M**., Chen ZX. and Breitman TR. **1998**. Potentiation of retinoic acid-induced differentiation of human acute promyelocytic leukemia NB4 cells by butyric acid, tributyrin, and hexamethylene bisacetamide. *Oncol. Res.* 10 (2):75-84.

7. Muccio DD., Brouillette WJ., Breitman TR., **Taimi M**., Emanuel PD., Zhang X., Chen G., Sani BP., Venepally P., Reddy L., Alam M., Simpson-Herren L. and Hill DL. **1998**. Conformationally defined retinoic acid analogues. 4. Potential new agents for acute promyelocytic and juvenile myelomonocytic leukemias. *J. Med. Chem.* 41(10):1679-87.

8. Parker BW., Kaur G., Nieves-Neira W., **Taimi M**., Kohlhagen G., Shimizu T., Losiewicz MD., Pommier Y., Sausville EA. and Senderowicz AM. **1998**. Early induction of apoptosis in hematopoietic cell lines after exposure to flavopiridol. *Blood* 91(2):458-65.

9. **Taimi M**. and Breitman TR. **1997**. N-4-hydroxyphenylretinamide enhances retinoic acid-induced differentiation and retinoylation of proteins in the human acute promyelocytic leukemia cell line,

NB4, by a mechanism that may involve inhibition of retinoic acid catabolism. *Biochem. Biophys. Res. Commun*. 232 (2):432-436.

10. **Taimi M**. and Breitman TR. **1997**. Growth, differentiation, and death of retinoic acid-treated human acute promyelocytic leukemia NB4 cells. *Exp. Cell. Res.* 230 (1):69-75.

11. **Taimi M**., Dornand J., Nicolas M., Marti J. and Favero J. **1994**. Involvement of CD4 in interleukin-6 secretion by U937 monocytic cells stimulated with the lectin jacalin. *J. Leukoc. Biol.* 55 (2):214-20.

12. Cellier MF., **Taimi M.**, Chateau MT., Cannat A. and Marti J. **1993**. Thermal stress as an inducer of differentiation of U937 cells. *Leuk. Res.* 17 (8):649-56.

13. **Taimi M**., Defacque H., Commes T., Favero J., Caron E., Marti J. and Dornand J. **1993**. Effect of retinoic acid and vitamin D on the expression of interleukin-1 beta, tumour necrosis factor-alpha and interleukin-6 in the human monocytic cell line U937. *Immunology* 79 (2):229-35.

14. **Taimi M.**, Defacque H., Commes T., Favero J., Dornand J. and Marti J. **1993**. The retinoic acid analog CBS-211A potentiates the 1 alpha,25-dihydroxyvitamin D3-induced differentiation of U937 cells. *Agents Actions* 38 (1-2):91-9.

15. **Taimi M**., Chateau MT., Cabane S. and Marti J. **1991**. Synergistic effect of retinoic acid and 1,25-dihydroxyvitamin D3 on the differentiation of the human monocytic cell line U937. *Leuk Res.* 15 (12):1145-52.

16. **Taimi M**., Chateau MT., Marti J. and Pacaud M. **1990**. Induction of differentiation of the human histiocytic lymphoma cell line U937 in the absence of vimentin expression. *Differentiation* 45 (1):55-60.