

# CHRISTOPHER TUDAN Ph.D.

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## PROFILE

A creative, organized and energetic scientist/Study Director possessing diverse experience in biochemical, bioanalytical (including LC/MS/MS), cellular and pharmaceutical sciences within the biotech/biopharmaceutical industry. A proven track record in leading early and late-stage drug development and pre-clinical programs. Managed numerous collaborations and contract research in diverse drug development and delivery programs meeting GLP/cGMP/OECD compliance. Functioned as GLP Study Director and methods development/validation scientist (bioanalysis and ADME), as well related project and team management. Familiar with developing and implementing business plans and related client-building strategies. Competencies include:

- Drug Development (target ID, validation, screening, lead optimization).
- LC/MS/MS method development and validation including GLP-compliant P450.
- Assay Development: Functional, Specificity, Lead Optimization, ADME, P450 and Bioanalytical (including LC/MS/MS), immunoassays and bioconjugation.
- Related Med/High Throughput including all current chemistries.
- Structure Activity Relationship (SAR) development.
- Project Leader and GLP project Study Director familiar with GLP, cGMP, OECD and ICH guidelines, and preparing all relevant documentation
- Excellent leadership and communication skills at multiple levels and disciplines. Motivated by opportunities to work with diverse teams.

## CAREER HISTORY

### **BioAccurate Enterprises, Inc.**

#### **Scientific Support – Bioanalysis, GLP-compliant Method Development/Validation, QA**

Advise, develop and validate LC-MS/MS and LBA methods, write protocols, conduct CRO site audits, coordinate client/CRO projects, analyze bioanalytical data, including GLP studies. Manage outsourced Bioanalytical programs for Sponsor. Instruct companies in Bioanalysis in the GLP lab – a technical perspective. Contracts include partnerships with Eli Lilly, ELANCO, Apollo R&D, Procyon Pharmaceuticals and Ricerca.

### **Advion BioSciences Inc**

**Oct 2004 – Sept 2006**

#### **Research Scientist / Study Director**

#### **BioAnalytical Department**

*Developed and validated LC/MS/MS and extraction methods for clinical and pre-clinical GLP studies and functioned as P.I. with direct interactions with client and FDA/client during audits. Developed and validated GLP-compliant drug-drug interaction assays and presented at conferences topics relevant to service and technology (Triversa).*

- Wrote relevant Protocols, Analytical Methods and Summaries, Final Reports, and SOPs for contractual analytical studies as a Study Director.
- Developed and implemented business plan for new GLP drug-drug interaction services. Increased processes through introduction of HTS methods, new technologies and

leadership. Develop research programs and collaborations to facilitate additional services including GLP-compliant LC-MS/MS P450 screening.

**Eli Lilly Canada (*Contract Position*)**

**2003 – 2004**

**Associate Senior Scientist - Bioanalytical Department**

*Responsible for method development and validation according to GLP guidelines, maintain HPLC and LC/MS/MS (SCIEX 3000/4000) sample analyses of defined clinical projects, integrate, compile, and review data and reports in a GLP environment. Member of internal GLP/SOP team.*

**Chemokine Therapeutics Corp**

**2000 - 2002**

**Director of Biology - Stem Cell Therapeutics and Cancer/MS Division**

*Responsible for developing Medium/High Throughput biological assays to assess small molecule libraries and rationally designed peptides for chemokine/receptor mimetics and antagonists. Managed Biology and Stem Cell Research Depts, and supported Chemistry Dept.*

- Implemented HTS radioligand binding assay to increase previous output 20-fold.
- Established biological assays to assess primary compound hits – resulted in identification of five small molecule compounds that were subsequently patented, with one undergoing clinical studies.
- Identified and assisted in development of SDF-1 agonists and antagonists for applications in stem cell therapeutics. Developed and managed pre-clinical studies - academic and CRO.
- Wrote 8 patents and responsible and one publications.
- Responsible for managing all collaborations and communications with legal representatives pertaining to patents and scientific advisory board.

**University of British Columbia**

**1999 - 2000**

**Post-Doc./Faculty Position - Faculty of Pharmaceutical Sciences**

*Responsible for elucidating the mechanism of CPPD/MSUM crystals in neutrophil activation associated with arthritis.*

- Identified PKC isoforms, PI-3K/Akt, PLC $\gamma$ 2 and ERK as mediators of neutrophil activity. Developed assays to study neutrophil apoptosis in the presence of crystals
- Identified that CPPD and MSUM crystals suppress TNF- $\alpha$ -induced and spontaneous apoptosis up stream of caspase 3, and is mediated by ERK and PI-3 kinase.
- Awarded Van Arman Awards from the Inflammation Research Association for research based on this project. Prepared and awarded Research Operating Grant from the Canadian Institutes of Health Research.

**BioChem Pharma Inc.**

**1996 - 1999**

**Research Associate**

**BioAnalytical / Cancer Biology Dept. - Supervisors: Dr. Terry Bowlin / Dr. Steven Pelech (Ph.D. supervisor)**

*Responsible for determining the mechanism of the angiogenesis inhibitor AGM-1470 and rationally-designed analogs. Also identified other therapeutic applications for these compounds. Team leader on project responsible for analyzing hepatocyte metabolism and stability of analogs, and distinguish between AGM-1470, metabolites and analogs in therapeutic efficacy.*

- Developed HPLC/PK assays to isolate angiogenesis leads and AGM-1470 analogs and metabolites.
- Developed novel HTS angiogenesis measuring multiple parameters.

- Generated an S.A.R. of AGM-1470 and analogs based on angiogenesis data.
- Developed a pharmacophore hypothesis of AGM-1470 and analogs based on HUVEC assays of AGM-1470 and 80 analogs to identify 5 novel compounds
- Demonstrated the molecular mechanism of AGM-1470 downstream of MetAP-2 followed by development of an applicable HTS assay.
- Determined that AGM-1470 is a putative therapeutic candidate for gouty arthritis and further established AGM-1470 and Taxol as anti-arthritis candidates.

**Montreal Neurological Institute**

**Jan. 1998- Feb. 1999**

**Industrial Post Doctorate Fellow / Scientist I**

**Cancer Biology Dept. / Brain Tumour Research Centre - Supervisor: Dr. David Kaplan**

*Given task of determining the signalling mechanisms involved in human glioma survival and proliferation with the paradigm that the target(s) should specifically target gliomas versus primary cells.*

- Identified a specific and selective glioma target that induces apoptosis in all gliomas but acts as a pro-survival factor in normal cells.
- Validated novel astrocyte/glioma target as potential anti-tumour and neurodegenerative drug target. Assisted in drafting relevant patent, research grant (awarded), and publication.
- Identified the role of TrkA as an inducer of apoptosis in human gliomas.
- Discovered a novel mechanism of Akt regulation which is independent of Ser/Thr phosphorylation and membrane localization, and ILK (PDK2) as a regulator of GSK-3 independent of Akt.

**Bristol-Myers Squibb**

**1988 - 1991**

**Research Associate/Intern - Metabolism and Pharmacokinetics Dept. HPLC analysis of preclinical plasma and brain samples relevant to adriamycin and taxol analogs, and etoposide pro-drugs. Honours thesis and full-time work during senior year.**

**EDUCATION**

Ph.D. Medicine – Experimental Medicine 1992-1999

University of British Columbia - Supervisor: Dr. Steven Pelech

Thesis title: *Mechanism of Fostriecin, AGM-1470 and Taxol disruption of cell cycle progression and cell activation.*

B.Sc. Chemistry (Honours – Cum Laude) 1988-1991

Southern Connecticut State University - Supervisor: Dr. Nathen Lerner

*the divalent entities -O-, -S-, -NH-, and -CH<sub>2</sub>- in rat plasma and PBS.*

**AWARDS**

Van Arman Excellence in Inflammation Research – Inflammation Research Assoc., September 2000.

MRC Studentship Award, 1992-1995.

Evelynn Martin Cancer Research Fellowship, 1992/93.

Honours graduate (Chemistry), 1991.

Alpha Chi Honors Society, 1990.

Chesborough Ponds Chemistry Scholarship for Highest Achieving Chemistry Student, 1990.

## SKILLS

- **Medium/High Throughput Assay Development:** Receptor binding, rapid liquid handling, chemotaxis, proliferation, kinase, calcium mobilization, angiogenesis, metabolism, cell-based, ELISA and bioconjugation techniques, pre-clinical directed functional assays. Knowledge of multiple screening, detection and material technologies for relevant applications.
- **Bioanalysis:** SPE and HPLC techniques for drug stability and metabolism analysis. LC/MS/MS method development and analysis to GLP compliance. FPLC fractionation for protein purification and characterization.
- **Pre-clinical studies:** Designed and managed (outsource to CRO) MTD, PK and efficacy (tumor, immunological, stem cell) studies, ADMET (including 96-well format).
- **GLP, cGMP, ICH Guidance:** Study director, team leader, LC/MS/MS method development and validation, dose analysis and sample analysis responsibilities using appropriate guidance's. Written study protocols (GLP), GLP methods, final reports, SOPs, and developed study programs for multiple biopharmaceutical companies. Interacted with clinical study directors as a CRO Study Director for multiple and challenging projects.
- **SAR Development:** Developed numerous Structure Activity Relationships, and established Lead compound criteria for scale-up. Assisted in several rational drug design programs based on SAR and molecular modeling.
- **Protein Biochemical Analysis:** *in vivo* and *in vitro* kinase and phosphatase activity analysis techniques, immunoaffinity assays including Western blotting, immunoprecipitation, ELISA, protein purification and analysis techniques including 2-D and gradient SDS-PAGE, HPLC, ion exchange, and TLC.
- **Apoptosis Analysis:** Based on DNA fragmentation, TUNEL, ELISA-based DNA fragmentation, caspase activity, and FACS analysis.
- **Cell Culture Techniques:** Primary and immortalized cells, immunofluorescence, immunohistochemical analysis, neutrophil isolation and respiratory activation determination methods, and cell-based assays.
- **Enzymology:** To assess binding, affinity, activity, competition, dose-effects (*in vitro* and *in vivo*), synergy/additive/antagonistic relationships (one versus two-site models), Km, and validation of P450 kinetics in microsomes for GLP-compliant assays.
- **Molecular Biology:** Subcloning and bacterial transfection and adenovirus infection methods in signal transduction analysis studies.
- **Project Leadership / Managerial Skills:** Manager of Method Development and Validation (*Exygen/MPI*), Director of Biology (*Chemokine Therapeutics*) and Project Leader in Oncology (*Cytochroma*). Leadership in numerous collaborations, such as Beth Israel Hospital (*Harvard*), Montreal Neurological Institute, Kinetek Technologies, BC Cancer Agency, Celator Technologies, Stem Cell Technologies, and Study Director (Advion), Team Leader and Study Director at two CROs, Manager of Method Development and Validation team.
- **Computer Skills:** Several LIMS systems, PRISM, Word, Excel, *Catalyst*, PowerPoint, PhotoShop and Illustrator, particularly with applications to data analysis, and presentations.
- **Excellent Writing and Presentation Skills:** Journals, patents, GLP regulatory and industrial research reports and SOPs. Exceptional communication skills, and experience with interacting in multidisciplinary and team settings.

## PATENTS

### 1. CXCR-4 Agonists Treatment for Hematopoietic Cells

Tudan, C., Merzouk, A., Arab, L., Eaves, C., and Cashman, J, Clark-Lewis, I., and Salari, H.  
WO 01/76615 A2 & US 2003/0148940 A1

2. **Therapeutics for Chemokine Mediated Diseases**  
Saxena, G., Tudan, C., Merzouk, A., Arab, L., and Salari, H.  
WO 02/45702 & US 2003/0069265 A1
3. **CXCR-4 Antagonists Treatment for Hematopoietic Cells**  
Tudan, C., Merzouk, A., Arab, L., Saxena, G., Eaves, C and Cashman, J., and Salari, H.,  
WO 01/85196 & Japan 099381
4. **IL-8 Receptor Antagonist – Drug for Inflammatory and Autoimmune Diseases**  
Saxena, G., Tudan, C., and Salari, H.  
US 6,515,001 B2
5. **Mip-1 $\alpha$  Receptor Antagonist – Drug for T-cell Mediated and Autoimmune Diseases**  
Saxena, G., Tudan, C., and Salari, H.  
WO 02/094270 A2
6. **RANTES Receptor Antagonist – Drug for Chronic Inflammatory and Autoimmune Diseases**  
Saxena, G., Tudan, C., and Salari, H.  
WO 02096397 & US 2003/0125380 A1
7. **Human Stromal-derived Factor (SDF) 1 $\alpha$ , SDF-1 $\beta$ , and SDF-1 Precursor Polypeptide Treatment of Hematopoietic Stem Cells and Hematopoietic Progenitor cells.**  
Tudan, C., Cashman, J., Eaves, C., and Salari, H.  
US 60/373,629
8. **Small Molecular Weight Aromatic Analogs as Chemokine Receptor Antagonists for CXCR-4 and/or SDF-1 Mediated Human Diseases, Autoimmune Diseases and in the Treatment of Hematopoietic Progenitor and Stem Cell Disorders**  
Saxena, G., Tudan, C., Cheng, N., and Salari, H.  
US 03/33792
9. **Inhibition of Rac as a Means to Selectively Suppress Astrocytoma Growth and Survival.**  
Tudan C., and Kaplan, D.  
Filed (PCT and US with BioChem Pharma and McGill University) 2000/2001

## PUBLICATIONS

1. **Cellular Signalling** 2004 Feb; 16(2):211-221  
*Calcium Pyrophosphate Dihydrate Crystal-associated Induction of Neutrophil Activation and Repression of TNF- $\alpha$ -induced Apoptosis is Mediated by the p38 MAP Kinase.*  
Tudan C, Jackson JK, Higo TT, Hampong M, Pelech SL, Burt HM.
2. **Inflammation Research** 2003 Jan; 52(1):8-17  
*The Effect of Inhibiting Topoisomerase I and II on Neutrophil Respiratory Burst and Apoptosis Responses.*  
Tudan C, Jackson JK, Higo TT, Burt HM.
3. **Oncogene** 2002 Nov 7; 21(51):7891-7896  
*The Rb-family protein p107 inhibits translation by a PDK1-dependent mechanism.*  
Makris C, Voisin L, Giasson E, Tudan C, Kaplan DR, Meloche S.
4. **Journal of Medicinal Chemistry** 2002 May 9; 45(10):2024-2031  
*Rational Designing of CXCR-4 Agonists: Novel Cyclam Derivatives of Stromal Cell-derived Factor (SDF-1). Chemical Synthesis of SDF-1 and its Analogues by Fmoc Strategy.*  
Tudan C,\*\* Merzouk A, Arab L, Chahal S, Willick GE, Law P, Salari H, and Merzouk A.
5. **Cancer Research** 2002 Apr 1; 62(7):2131-2140  
*Suppression of Rac activity Suppresses Apoptosis in Human Glioma Cells but not Normal Human Astrocytes.*  
Senger D, Tudan C, Guiot M-C, Mazzoni, IE, MolenKamp G, LeBlanc R, Antel J, Snipes GJ, Snipes WJ, and Kaplan D.
6. **Inflammation Research** 2002 Feb;51(2):105-107  
*CPPD crystal-induced suppression of neutrophil apoptosis is regulated by the ERK1/2 and PI3-kinase/Akt pathways.*  
Tudan C, Jackson JK, Burt H.

- 7. 2nd International Peptide Symposium/17<sup>th</sup> American Peptide Symposium 2001**  
**Proceedings** June 2001  
*Rational Designing of CXCR-4 Agonists and Antagonists: Synthesis of Novel Cyclam Derivatives of Stromal Cell-derived Factor (SDF-1).*  
 Merzouk A, Tudan C, Arab L, Chahal S, Willick GE, and Salari H.
- 8. J. Immunology** 2000 Nov 15; 165(10): 5798-5806  
*Inhibition of TNF- $\alpha$  induced neutrophil apoptosis by crystals of calcium pyrophosphate dihydrate in mediated by the ERK and PI-3K/Atk pathways upstream of caspase 3.*  
Tudan C, Jackson JK, Pelech SL, Burt HM.
- 9. J. Rheumatology** 2000 Oct; 27(10): 2463-2472  
*The inhibition of spontaneous and TNF- $\alpha$  induced neutrophil apoptosis by crystals of calcium pyrophosphate dihydrate and monosodium monohydrate.*  
Tudan C, Fong D, Duronio V, Burt HM, Jackson JK.
- 10. J Rheumatology** 2000 Dec; 27(12): 2877-2885  
*The Involvement of PLC in Crystal Induced Neutrophil Activation.*  
 Jackson JK, Tudan C, Burt, HM.
- 11. Biochemical Pharmacology** 1999 Dec; 58: 1869-1880  
*AGM-1470 Selectively Inhibits Protein Kinase C, MAP Kinase and Neutrophil Activation in Response to CPPD Crystals, fMLP and Phorbol Ester.*  
Tudan C, Jackson JK, Pelech SL, Attardo G, Burt HM.
- 12. J Neuroscience** 1999 Sept 6; 146(5) 955-966  
*Depolarization and Neutrophins Converge on the PI 3-kinase-Akt Pathway to Synergistically Regulate Neuronal Survival.*  
 Vaillant A, Mazzino I, Tudan C, Boudreau M, Kaplan D, Miller F.
- 13. Biochemical J** 1998 Apr 15; 331 (Pt 2) 531-537  
*Activation of S6 kinase in Human Neutrophils by Calcium Pyrophosphate Dihydrate Crystals: Protein Kinase C-dependent and Phosphatidylinositol-3-kinase-independent Pathways.*  
Tudan C, Jackson JK, Charlton K, Pelech SL, Sahl B, Burt HM.
- 14. J Immunology** 1997 Apr; 90(4) 502-510  
*Calcium Pyrophosphate Dihydrate Crystals Activate MAP Kinase in Human Neutrophils: Inhibition of MAP Kinase, Oxidase Activation and Degranulation Responses of Neutrophils by Taxol.*  
 Jackson JK, Tudan C, Sahl B, Pelech SL, Burt HM.
- 15. EMBO J** 1995 Mar 1; 14(5) 976-985  
*Chromosome Condensation Induced by Fostriecin does not Require p34cdc2 Kinase Activity and Histone H1 Hyperphosphorylation, but is Associated with Enhanced Histone H2A and H3 Phosphorylation.*  
 Guo XW, Th'ng JP, Swank RA, Anderson HJ, Tudan C, Bradbury EM, Roberge M.
- 16. Cancer Research** 1994 Dec; 54 (23) 6115-5121  
*Antitumour Drug Fostriecin Inhibits the Mitotic Entry Checkpoint and Protein Phosphatases 1 and 2A.*  
Tudan C\*, Roberge M\*, Hung SM, Harder, KW, Jirik, FR, Anderson H.

## ASSOCIATIONS

Society of Quality Assurance, AAAS, AAPS, ACS, Inflammation Research Association, Associate Editor for J. Biomolecular Screening, Society for Biomolecular Screening,

## INTERESTS

Sailing (racing), SCUBA diving (Dive Master), Rowing, Tennis, Golf, Climbing and Amateur Astronomy.

## **REFERENCES**

Key, world recognized members of the scientific, academic and biotechnology community will act as references on my behalf when a mutual opportunity is identified. Client references from Eli Lilly, Bristol-Myers Squibb, ELANCO, and Procyon Pharmaceuticals, to name a few, also available upon request, as well as colleagues from CROs leading bioanalytical programs, and QAU.