

CURRICULUM VITAE

Anil Koul



Coremannstraat 2
2600, Berchem, Belgium

Phone: +32 14603420 (office)
+ 32485796193 (Mobile)

E. mail: anilkoul30@yahoo.com

Summary

- Group leader in research and development with more than 3 years of work experience in a biotechnology company.
 - Heading a project team involved in developing kinase inhibitors as anti-infective agents.
 - Excellent knowledge and skills in pre-clinical development of a drug candidate, right from target identification, assay development to animal models.
 - A good team player with excellent communication skills, experience in strategic planning and project management.
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Personal Information

Citizenship: Indian
Marital Status: Married, one daughter

Education

Ph.D. (Molecular Biology): Max Planck Institute for Biochemistry, Munich, Germany;
Institute for Genomics and Integrative Biology, Delhi;
Department of Biochemistry, University of Delhi, India (1996-2000).

M.Sc: Department of Zoology, University of Delhi, India (1993-1995)

Professional experience:

Current employer: Since September 2004

Johnson and Johnson, pharmaceutical and research, Belgium

Position: **Senior scientist, Project Team Leader**

Department: **Antimicrobial drug discovery**

Project Team Leader*March 2002 - present*

Axxima Pharmaceuticals AG, Munich, Germany

Projects: Target validation and development of kinase inhibitors as novel anti-bacterial and anti-viral agents

Responsibilities:

As project team leader, I manage the entire anti-TB program - this involves target identification and validation, high throughput screening, lead optimisation and pre-clinical development. Based on a matrix structure I interact with assay and screening department, IP department, and computational and medicinal chemists.

- Managing 4 external collaborations. Responsible for cooperation's with other companies (e.g. Novartis, NITD, Singapore, Vichem, Budapest) and academia (e.g. Prof. J. Pieters, Univ. Basel, Switzerland)
- Validated a mycobacterial kinase, as a critical gene for mycobacterial virulence.
- Analysis of mode of action of the target kinase. Discovered the mode of action of the mycobacterial target kinase (please see publication).
- Screening of target with Axxima's kinase biased library and identification of AX14585, a promising candidate for the clinical development (please see patent application).
- AX14585 and its analogs are currently in the medicinal chemistry optimisation process.
- We identified novel, broad antibacterial and anti-viral compounds belonging to Axxima's proprietary scaffold consisting of 500 in-house compounds. Several compounds were tested as potent inhibitors of Influenza virus replication, HIV and TB.

Scientist*May '01- August '02*

Axxima Pharmaceuticals AG, Munich, Germany

Tasks performed:

- Identification and validation of host and mycobacterial kinases as novel drug targets.
- Micro-array analysis of changes in the gene expression profile of macrophages upon infection with pathogenic bacteria.
- Identification of host kinases up-regulated upon bacterial and their role in bacterial pathogenesis by using RNAi techniques.
- Development of biochemical and cell based assays for high throughput screening

Further management training

Axxima Pharmaceuticals

- A certificate in Project Management by the International Institute of Learning, Inc. (www.iil.com), at Frankfurt, April - May '03.

Post-Doctoral experience

Max-Planck Institute for Biochemistry and Axxima Pharmaceuticals, Martinsried, Munich (www.biochem.mpg.de)

- Post-doctoral fellow in the laboratory of Prof. Axel Ullrich at Max-Planck Institute for Biochemistry, in Martinsried, Munich.
- Project: Kinases and bacterial pathogenesis

Doctoral work

- Ph.D student in the laboratory Prof. Yogendra Singh at Institute for Genomics and Integrative Biology, Mall Road, India.
- Worked in laboratory of Prof. Axel Ullrich at Max-Planck Institute for Biochemistry, in Martinsried, Munich.

Patents

- Secretory tyrosine phosphatases of mycobacteria.
Ullrich A and Koul A (2000) (Max-Planck Institute for Biochemistry, - WO 01/81422 A1)
- 4,5,6,7-Tetrahydrobenzo- (b)-thiophene derivatives and methods for medical intervention against mycobacterial infections.
Koul A., Choidas, A., Missio A., Bacher G (2002) (Axxima Pharmaceuticals WO 03/084947 A1)
- Benzo [g] quinoxaline derivatives as effective compounds against infectious diseases.
Koul A et al, (Axxima Pharmaceuticals, 2002 : WO 02/094796).
- 4,7-Dihydro-5H-thieno [2,3c] pyran derivatives and their analogues as effective compounds against infectious diseases.
Koul A et al., (Axxima Pharmaceuticals; 2003

Publications

- **Koul A***, Herget T., Klebl B and Ullrich A (2004). Interplay between mycobacteria and host signalling pathways.
Nature Reviews Microbiology 2, 189 -202. * *Corresponding author*

- Anne Walburger*, **Anil Koul***, Giorgio Ferrari*, Liem Nguyen, Bert Klebl, Charles Thompson, Gerald Bacher and Jean Pieters (2004). The eukaryotic-like Serine/Threonine kinase G from pathogenic mycobacteria mediates mycobacterial survival in macrophages. **Science** Vol 304,1800-04 . *Equal contributors.
- Chopra P., Vohra R., Meena L., **Koul A.**, Tyagi A K and Singh Y (2004). Nucleoside diphosphate kinase of *M. tuberculosis* acts as GTPase-activating protein for Rho-GTPases. **FEBS Letters** (accepted).
- Chopra P., Singh B., Singh R., Vohra R., **Koul A.**, Meena L., Deol P., Tyagi A K and Singh Y (2003). Phosphoprotein phosphatase of *Mycobacterium tuberculosis* dephosphorylates Serine/threonine kinases PknA and PknB. **BBRC**, 311(1):112-20
- Singh R., Rao V., Shakila H., Gupta R., Khera A., Dhar N., **Koul A.**, Singh Y., Naseema M., Narayanan P K., Paramasivan CN. Ramanathan V D and Tyagi AK (2003). Disruption of *mptb* impairs the ability of *Mycobacterium tuberculosis* to survive in host. **Mol. Microbiol.** 50(3):751-62.
- Chopra P., Singh A., **Koul A.**, Ramachandran S., Drlica K., Tyagi A K and Singh Y (2003). Cytotoxic activity of nucleoside diphosphate kinase secreted from *Mycobacterium tuberculosis*. **Eur. J. Biochem**: 270 (4) :625-34
- **Koul A.**, Choidas A., Tyagi A K., Drilica K., Singh Y and Ullrich A (2001) Serine/Threonine protein kinases PknF and PknG of *Mycobacterium tuberculosis*: Characterization and Localization. **Microbiology** 147: 2307-14
- **Koul A.**, Choidas A., Treder M., Tyagi A K., Drilica K., Singh Y and Ullrich A (2000). Cloning and characterization of secretory tyrosine phosphatases of *Mycobacterium tuberculosis*. **J Bacteriol.**, 182: 5425-32
- Jain N K and **Koul A** (1996). Laboratory diagnosis of pulmonary tuberculosis (1996): Conventional and newer methods. **The cardio-thoracic journal** (2): 5

Fellowships and Awards

- An academic exchange fellowship by the German Academic Exchange Service (Deutscher Akademischer Austauschdienst, <http://www.daad.de>) 1998-2000.
- Qualified for a national fellowship from the Council for Scientific and Industrial Research, India (www.csir.res.in), 1995-1997.
- A fellowship to study at 'Centre for Advanced studies-Zoology' University of Delhi, 1993-1995.

Knowledge/ Experience:

Molecular Biology

- Broad anti-bacterial drug-screens including mycobacteria, *E. coli* EHEC, and other bacterial growth assays.
- Growth assay using bacterial reporter strains.
- Cellular infection assays using *Legionella*, *Mycobacteria* and *E. coli* etc.
- Immunofluorescence - Phagosomal-lysosomal localisation.
- Microarray and RNAi technologies - Identifications of bacterial and host cell targets.
- Allelic exchange mutagenesis for creation of bacterial gene knock-outs.
- Organelle electrophoresis - isolation of phagosomes etc.
- Cloning, PCR, RT-PCR, Tag-Man analysis of gene expression.
- Protein purification techniques using Chromatographic techniques, gel filtration, ion exchange, affinity chromatography. Detergent extraction of membrane proteins, SDS PAGE, Native gels, Activity Gels.
- Immunological techniques include immunizing laboratory animals, Western Blotting, ELISA, purification of antibodies.

- Immunoprecipitation etc.

Assay development.

- Assay development for identified targets.
- Kinase and phosphatase assays using cellular and recombinant kinases.
- *In vitro* transcription and translation assays.
- *In vivo* labelling.
- Dormancy / Latency bacterial assays.

Lead optimisation:

- Running lead optimisation cycles for the hits identified in high throughput screens.

Pre-clinical development:

- Solubility and metabolic stability (using human and mouse liver microsomes) assays.
- Mouse Irwin grid model. Maximum tolerated dosage determination.
- Pharmacokinetic studies in mice.
- Mice infection assays.
- Other early ADMET assays.

Cellular Biochemistry

- Tissue culture experience in primary cell cultures, radioactive and non-radioactive, Cytokine level estimations in test serums and primary cultures, transfections, generation of monoclonal stable cell lines.
- Developed methodologies for siRNA delivery and screening in mammalian cells

References

- *Prof. Jean Pieters*, Biozentrum, University of Basel
Klingelbergstrasse 50/70
CH-4056 Basel / Switzerland
Tel: 00-41-61.2671494
Email: jean.pieters@unibas.ch
- *Prof. Yogendra Singh*
Institute of integrative biology and genomics
Mall road, Delhi, India 110007
Tel: 00-91-11-7666156
Email: ysingh@cbt.res.in
- *Prof. Anil Tyagi*,
University of Delh , South campus
Delhi, India
Email.akt1000@hotmail.com
- *Prof. Thomas Herget*,
Merck KGaA,
Frankfurter Str. 250,
D-64293 Darmstadt, Germany.
Tel: 00-49 –61-51 72-0
Email: Thomas.herget@merck.de