

COST ACTION B22
DRUG DEVELOPMENT FOR PARASITIC
DISEASES

COST B22 WG2: Drug target characterisation

Venue

University of Glasgow
Glasgow G12 8QQ
Glasgow UK

Local organisers

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DATE: May 7-9, 2006

Plans for Expert Group Meeting – ‘Protein kinases involved in cell proliferation, differentiation and homeostasis: targets for anti-parasitic chemotherapy’

It has been agreed that this meeting of the WG will cover protein kinases involved in cell proliferation, differentiation and homeostasis, with an emphasis on targets for anti-parasitic chemotherapy

Context and Rationale

Eukaryotic protein kinases (ePKs) play a central regulatory role in many cellular processes, including cell cycle control, development, morphogenesis and cellular homeostasis. The majority of studies ePKs have focused on model organisms; however, the recent elucidation of the ePK repertoire for a number of parasitic protozoa has opened up new avenues of research for studying cellular regulatory mechanisms in lower eukaryotes.

Deregulation of protein phosphorylation is at the origin of several pathologies (e.g. cancers and neurodegenerative diseases), and ePKs are now considered as promising drug targets. Indeed, three kinase inhibitors have recently been made available on the market as anticancer agents, and several more are in clinical trial in the context of a variety of diseases. The **rationale** for targeting protein kinases of parasitic protists is based on the proposition (now confirmed in a number of well documented examples) that the vast phylogenetic distance between unicellular parasites and their vertebrate hosts is reflected by divergences in the properties of their protein kinases, which may be exploited for specific inhibition of the enzymes of the parasites.

The **objectives** of the meeting are twofold:

- (i) To bring together investigators working on protein kinases involved in regulating (1) cell proliferation, (2) differentiation and (3) cellular homeostasis (4) cell remodelling.
- (ii) to promote discussions with industrial partners on how to translate fundamental research data into drug discovery efforts

Timing and location

Arrival on the Saturday, sessions Sunday, Monday and Tuesday morning.

PROGRAMME

Saturday 6th May 2006

18.00-21.00 Arrival

Sunday 7th May 2006

9:15

Introduction

9:30 – 11:00

I Session PROTEIN KINASES AS DRUG TARGETS

Chair: Laurent Meijer

- **Christian Doerig** (UK): Targeting protein kinases of parasites and of their host cells: an overview.
- **Peter Fischer** (UK): Targeting the cell cycle and transcription for different therapeutic applications.
- **Laurent Meijer** (France): Inhibition of GSK3 in mammalian cells and in *Plasmodium falciparum*

11:00 – 11:30

Coffee break

11:30 – 13:00

II Session CMGC PROTEIN KINASES - biology

- **Martin Wiese** (Germany): From single kinases to signalling cascades.
- **Gerald Spaeth** (France): A transgenic approach to study MAP kinase functions during the *Leishmania* infectious cycle.
- **Norman Waters** (USA): Characterization of the regulatory mechanisms and chemical inhibitor profile of the malarial cyclin dependent protein kinase, Pfmrk.

13:00

Lunch

14:30 – 16:00

III Session CMGC PROTEIN KINASES – from biology to chemistry

- **Jeremy Mottram** (UK): Towards the identification of *Leishmania*-specific CDK inhibitors.
- **Karen Grant** (UK): Anti-leishmanial activity of indirubins: development of parasite-selective CDK inhibitors.
- **Nick Westwood** (UK): Novel Indirubin analogues as inhibitors of parasite CDKs.

16:00 – 16.30

Coffee break

16:30 – 18:00 **IV Session CMGC PROTEIN KINASES – structure**

- **Jane Endicott** (UK): Structural studies and implications for inhibitor design.
- **Malcolm Walkinshaw** (UK): CDK2: from structure to function.
- **Paul Selzer** (Germany): Virtual screening of a CDK from *Eimeria tenella*.

19:30 **Dinner**

Monday 8th May 2006

09:30 – 10:30 **Special lecture**

- **CC Wang** (USA): The changing link between mitosis and cytokinesis in trypanosomes

10:30 – 11:00 **Coffee break**

11:00 – 13:00 **V Session AGC PROTEIN KINASES / cAMP SIGNALLING**

- **Puskar Sharma** (India): Protein kinase PfPKB constitutes a novel signaling pathway in malaria parasites
- **David Baker** (UK): The role of cGMP and cGMP-dependent protein kinase in *P. falciparum* sexual development.
- **Charles Jaffe** (Israel): Role of leishmanial protein kinase A in survival and virulence
- **Michael Bosshart** (Germany): The PKA-like kinase of *Trypanosoma brucei*

13.00 **Lunch**

14:30 – 16:00 **VI Session “OTHER PROTEIN KINASES (OPKs)”**

- **Tansy Hammarton** (UK): Polo-like kinase is essential for kDNA segregation and cytokinesis, but not mitosis in *Trypanosoma brucei*.
- **Luc Reininger** (UK): Functional characterisation of NIMA-like kinases in the human malaria parasite *P. falciparum*.
- **Derrick Robinson** (France): TbNRKC, a novel NIMA related kinase involved in basal body separation in *Trypanosoma brucei*.

16:00 – 16.30 **Coffee break**

16:30-18:00

VII Session “OTHER PROTEIN KINASES 2 (OPKs)”

- **Larry Ruben** (USA): *Trypanosoma brucei* Aurora kinase
- **Barbara Kappes** (Germany): Correct location for proper function: targeting of a *P. falciparum* calcium-dependent protein kinase to the parasitophorous vacuolar space.
- **Dominique Dorin** (UK) : A role for the PfPK7 protein kinase in asexual and sexual development of *P. falciparum*. (15 min)
- **Sylvain Eschenlauer** (UK) : *P. falciparum* Tyrosine kinase-like enzymes. (15 min)

19:30

Dinner

Wednesday 9th May 2006

9:00 – 11:00

VIII Session Signalling pathways

- **Kavita Shah** (USA): Chemical Genetic Dissection of Signaling Cascades
- **Dan Zilberstein** (Israel): Differentiation of *Leishmania donovani* in host-free system: analysis of signal perception and response
- **Tom Seebeck** (Switz.): Cyclic nucleotide-specific phosphodiesterases - novel drug targets that are highly conserved between host and parasite
- **Caroline Clucas** (UK): An RNAi screen for cell cycle regulators in *Trypanosoma brucei*

11:00 – 11:30

Coffee break

11:30 – 12:30 IX Session “aPKs AND PHOSPHATASES”

- **Mark Field** (UK): Functions of VPS34 in *Trypanosoma brucei*
- **Balazs Szoor** (UK): Protein tyrosine phosphatase TbPTP1: a molecular switch controlling life cycle differentiation in *Trypanosoma brucei*.

12:30 – 13:00

Closing remarks