



# **Systems Biology for Cancer Drug Development**

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# Introduction to Physiomics plc

- **Business**

- Founded 2001, Oxford (UK) based, listed on the LSE (AIM) 2004
- We use computer modelling to understand and predict optimal cancer therapy.
- We accelerate the discovery process and reduce development risk.

- **Focus**

- Cancer (one of only a handful of companies).
- Simulation drug Mechanism Of Action (MOA).
- Combination therapy and cell populations (SystemCell® Technology).

- **Collaborations:**

- Eli Lilly
- Cyclacel Pharmaceuticals
- ValiRx - Cronos Therapeutics
- Bayer Technology Services
- TEMPO (FP6 - EU LifeSciHealth project)
- Institute of Life Science, Swansea University (HPC)

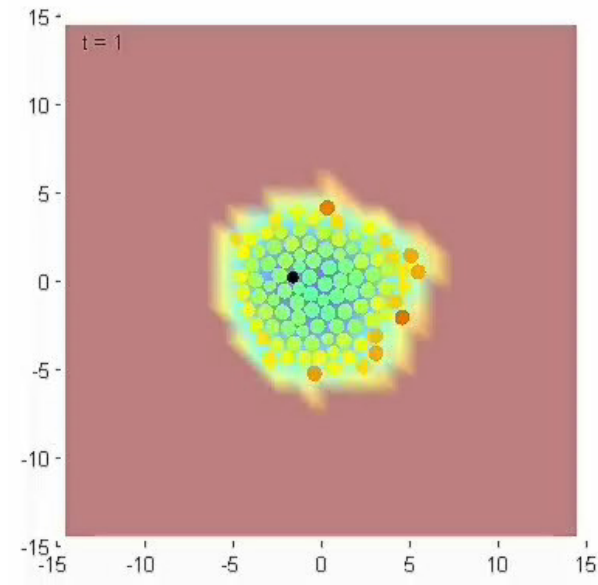
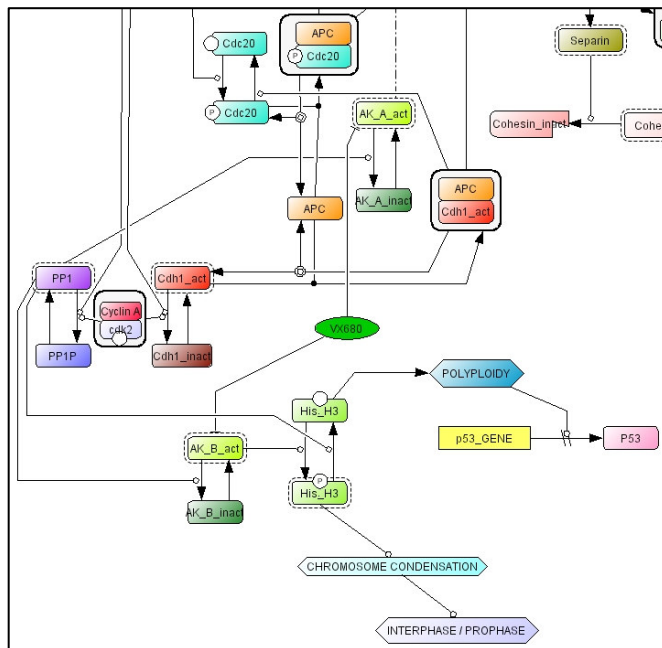


Bayer Technology Services



# Systems Modelling (Computer Simulation)

- “Systems biology seeks to understand complex biological systems in their entirety by integrating all levels of functional information into a cohesive model”<sup>1</sup>
- As drug discovery is moving towards the rational design of drugs based on a mechanistic understanding of biology, a systems [modelling] approach is becoming increasingly necessary<sup>2</sup>, particularly as systems can behave non-intuitively.



Click here to access the video

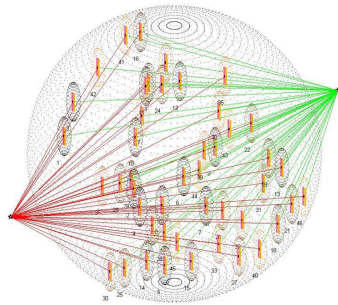
[www.physiomics-plc.com/virtual\\_tumour.htm](http://www.physiomics-plc.com/virtual_tumour.htm)

<sup>1</sup>Thiel, *Nature Biotechnology* 24,1055-1057 2006

<sup>2</sup>Araujo et al, *Nature Review Drug Discovery* 6, 871-880 2007

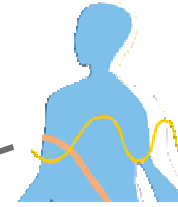
# Physiomics' Current Pharmacodynamic Models Portfolio

## Search & Capture



Mitotic poisons  
(e.g. taxanes) - - -

## Circadian clock (TEMPO)



Aurora kinase inhibitors

CDK inhibitors

Chemotherapy  
Radiotherapy



p53 family

IAP inhibitors

Caspase 9, 3 activation

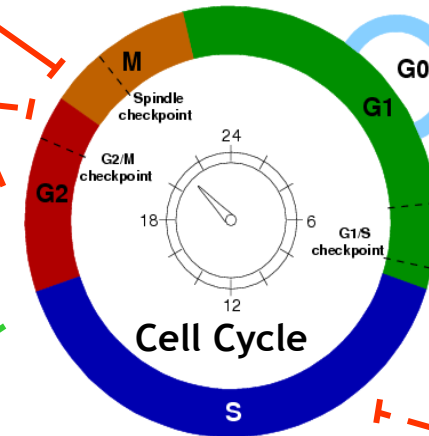
Mitochondrial permeability

bcl2 family

BH3 mimetics  
bcl2 inhibitors

mdm2 inhibitors  
pifithrin etc.

Nucleoside analogs

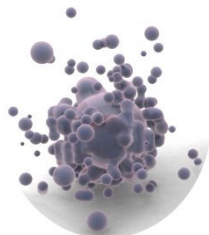


Growth factor

MAPKinase pathway inhibitors

restriction point

CDK inhibitors



APOPTOSIS

# Physiomics' Unique Sales Proposition

- *Cancer focused* (one of only a handful of companies).
- Detailed models of cellular biochemistry and drug pharmacology *based on prior knowledge* to support rational decision making.
- *Market-driven* development of technology to address specific key issues:
  - **Target Validation** - support “go” or “no-go” decisions for different possible drug targets, either alone or in combination
  - **Lead Selection** - support “go” or “no-go” decisions for different possible drug candidates early in the discovery phase
  - **Combination therapy** - support decisions for potential combinations of developmental and licensed drugs
  - **Chronotherapy** - predict optimal dosing times for different drugs
  - Illustrate **Mechanism of Action** for laboratory results that can be used to support patent applications and to gain regulatory approval (FDA “critical path”, EMEA new recommendations Sep 2007)<sup>1</sup>
  - **Effects of different genotypes** - patient stratification

<sup>1</sup> Schneider et al, Nature Review Drug Discovery 7, 893-899 2008

# History of Physiomics

**2001:** VC Funding; Scientific Direction from Prof. David Fell (Oxford Brookes Uni.)

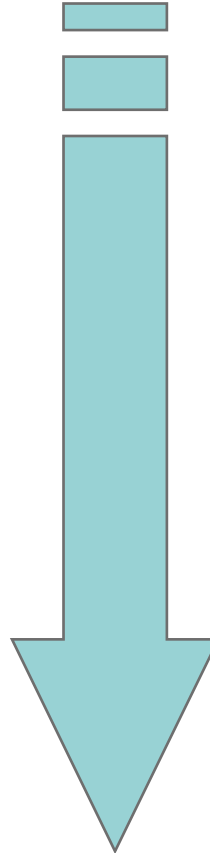
**2002:** First collaboration with Cyclacel Pharmaceuticals Ltd. from networking.

**2004:** Listed on LSE (AIM) to raise £750k. Continued projects with Cyclacel. Collaboration with Bayer Technology Services.

**2006:** First placement since IPO (£429k) Started EU FP6 project, TEMPO.

**2007/2008:** Refocusing of business, recruitment of new team and board changes. Collaborations with Eli Lilly and ValiRx. MOU signed with Swansea University, Institute of Life Sciences.

## Formation



## Present

Purchased and developed cell population software, “SystemCell®”.

Constructed initial cell cycle model.

Integrated cell cycle model with cell population modelling software.

Adopted “PK-Sim®” for PK modelling.

Developed models to include details around more drug targets. Created “Virtual FACS” technology.

Constructed apoptosis model. Constructed PK/PD Chronotherapy Model. Acquired access to IBM “Blue C” HPC at ILS, Swansea Uni. Created “Virtual Tumour” technology. Technology Out-Licensing “Model Player”

# Current Management Team

- **Chairman: Dr Paul Harper**

Dr Paul Harper has over 30 years' experience in the life sciences industry covering both drug development and medical devices. Paul has served as Chief Executive of Cambridge Antibody Technology Limited, and Provensis Limited. He has also served as Corporate Development Director of Unipath Limited, then the medical diagnostics business of Unilever PLC, and as Director of Research and Development for Johnson & Johnson Limited. Formerly head of Antimicrobial Chemotherapy for Glaxo PLC, Paul has a PhD in Molecular Virology and is the author of over 50 publications.

- **Chief Operating Officer: Dr Christophe Chassagnole**

Dr Christophe Chassagnole has been involved in bio-computing projects during the 14 last years, with experience in both academic and industrial environments. His Doctorate was achieved at the Victor Segalen-Bordeaux II University, and then he held a post doctorate position with IBVT at Stuttgart University. Before Joining Physiomics Dr Chassagnole worked in France as a senior researcher for CRITT Bio-Industries (Toulouse) for 3 years. He joined Physiomics in May 2004 as project leader to develop the model portfolio of the company. He was appointed Chief Operating Officer of Physiomics in May 2007.

- **Chief Scientific Officer: Professor David Fell**

Prof David Fell is Assistant Dean of the School of Biological and Molecular Sciences at Oxford Brookes University and is recognised as an expert in systems biology. Professor Fell runs a research team at Oxford Brookes University where current projects include the analysis of the structure of metabolic networks, the computer simulation of signal transduction and elementary modes for the analysis of metabolism and metabolic engineering. He is the author or co-author of approximately 85 scientific publications and has written one of the standard textbooks, "Understanding the Control of Metabolism" in the area of metabolic control analysis. Professor Fell has been involved with the Company since 2001.

- **Financial Controller: Mr Roger Jones**

Mr. Jones has for 30 years been a Fellow of the Association of Chartered Certified Accountants and has held a number of senior financial positions and key roles in biotechnology and pharmaceutical companies including Cambridge Antibody Technology, Onyvax, Archimedes Pharma, Angel Biotechnology and Provensis.

- **Business Development: Mr Gavin Clark**

Gavin Clark has 25 years experience in the life sciences sector holding senior positions in the industry before forming his own practice Procera Partners Limited. He was responsible for Global Licensing for infectious diseases at Glaxo Wellcome until 1999 and served as VP Business Development for Tibotec Pharmaceuticals up until the acquisition by Johnson & Johnson in 2002. His extensive licensing & commercial development experience encompasses Global, Regional, Drug Delivery, Diagnostics and Generics deals from both big and small sides of the negotiating table. Mr Clark has a bachelors degree in Chemistry from the University of Strathclyde.



# Business Model

- **Fee-for-service (perform modelling on demand):**
  - Developed proof-of-concept and testimonials from previous & current collaborations (Cyclacel, ValiRx, Eli Lilly)

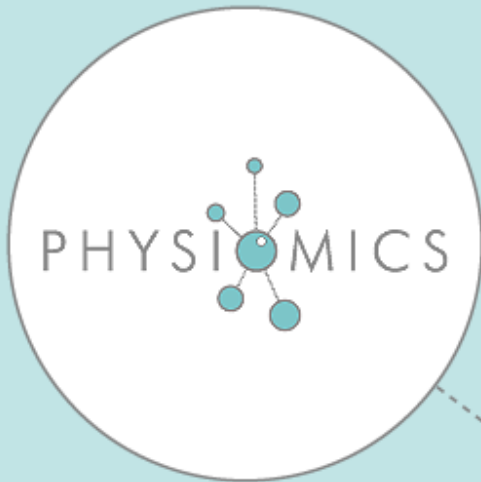
*“Physiomics’ service and technology is absolutely superb, we have just had some work carried out and it has saved us very significant amounts of development money and time. This is the first time the research has been done this way.....”* George Morris, CDO, ValiRx (Sept. 2007)

- Developed technology for many anti-cancer drug targets.
- **Shared risk/IP:**
  - Co-development and shared risk for IP.
  - Drug “rescue” or repurposing.

TEMPO EU FP6 project: Design of optimal chronotherapeutic schedules for Irinotecan and Seliciclib through modelling.

# Summary

- Computer models of cell proliferation and cell death (cancer).
- Technology developed for many anti-cancer drug targets.
- Developed over many years (since 2001), specifically driven by the market (specialised proprietary cell population simulations, “SystemCell<sup>®</sup>” and “Virtual Tumour”).
- Proven benefits with small and large pharmaceutical companies:
  - **Increase efficiency of research effort**
  - **Increase probability of success**
    - ⇒ **Reduce cost**



**Thank You**

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