



Institute of  
Pharmaceutical  
Innovation

# The IPI

*Delivering solutions in Drug Development*



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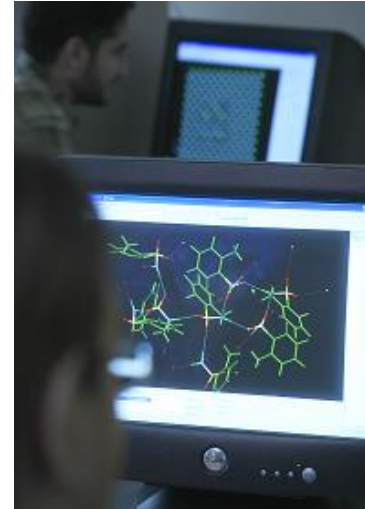


GOVERNMENT OFFICE  
FOR YORKSHIRE AND THE HUMBER



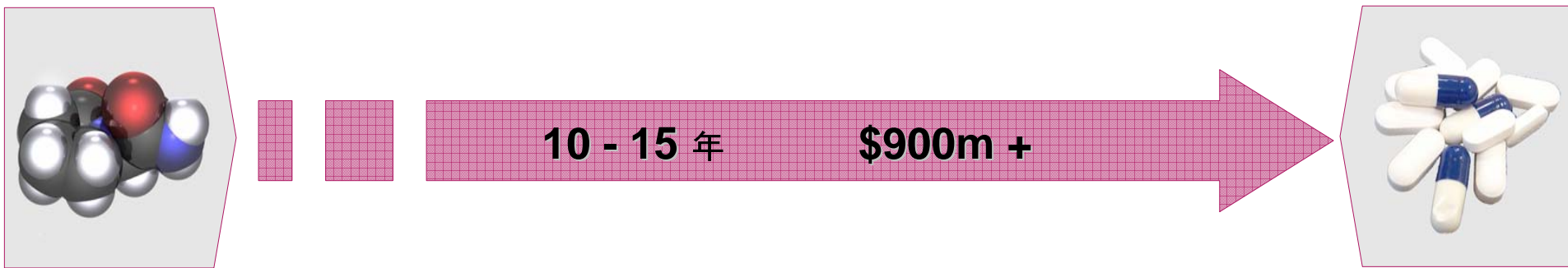
# Introducing the IPI

- The challenge of drug development  
新药开发的挑战
- The IPI vision  
IPI 的理念
- How the IPI operates  
IPI 如何运作
- The IPI as a Centre for Industrial Collaboration  
IPI是一个工业合作中心
- The IPI as a Centre for Innovation  
IPI是一个创新中心
- Our research scope  
我们的科研领域
- China interactions  
与中国的交流



# The challenge of drug development

## 新药开发的挑战



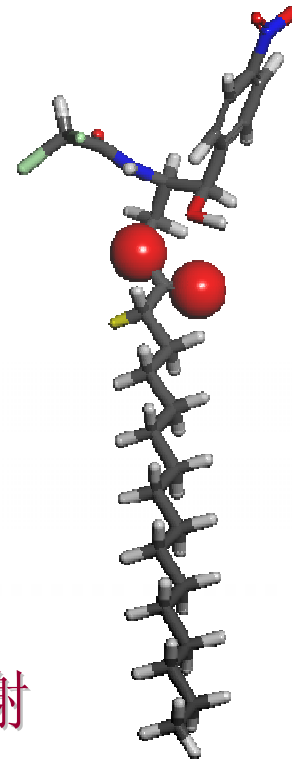
- **75% of the cost of developing a drug is paying for failures**  
75% 的新药开发费用花在失败上
- **Even when launched, many drugs have sub-optimal profiles**  
即使成功推出，很多新药仍有许多方面需要优化和改良

**There are significant benefits to patients and industry  
in finding ways to address these issues**

找到解决这些难题的方法对病人和制药企业都具有深远意义

# 41% of Drug Failures are due to poor biopharmaceutical properties

- Solubility 可溶性
- Stability 稳定性
- Permeability 渗透性
- First-pass metabolism 一级代谢





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# The IPI vision

- A research centre of excellence in predictive pharmaceuticals, focused on accelerating drug development  
一个擅长于预测制药学的研究中心，致力于加快医药研发的速度
  - Product development (formulation and delivery systems)
  - Solid-state pharmaceutical materials and particle science
  - A special emphasis on 'in-silico' methods (e.g. AI)
- An international centre for commercialisation  
一个国际商业化中心
  - In collaboration with our partners in UK Government in industry and the National Health Service



***Delivering solutions in drug development***

# IPI Building and facilities

Level 4  
Bioincubator Suite  
Offices & Labs

Level 3  
Pharmaceutical &  
Bio-analysis Labs

Level 2  
High Performance  
Computing

Level 1  
Formulation Science  
Labs (& Networking)

Level 0  
Materials Analysis

Level -1  
Structure Analysis





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# IPI 研究院的构成

五楼  
商业孵化器

四楼  
制药，生化实验室

三楼  
高性能运算中心

二楼  
合成药剂实验室

一楼  
材料分析

负一楼  
结构分析





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# How the IPI operates

- A world-class academic research centre  
世界级科研中心
  - Addressing unmet market need
  - Professional and delivery focused
- A Centre for new Bioscience Businesses  
新生物科学中心
- A UK government-accredited Centre of Industrial Collaboration  
英国政府授权的工业合作中心





# Key Areas for Industrial Collaboration

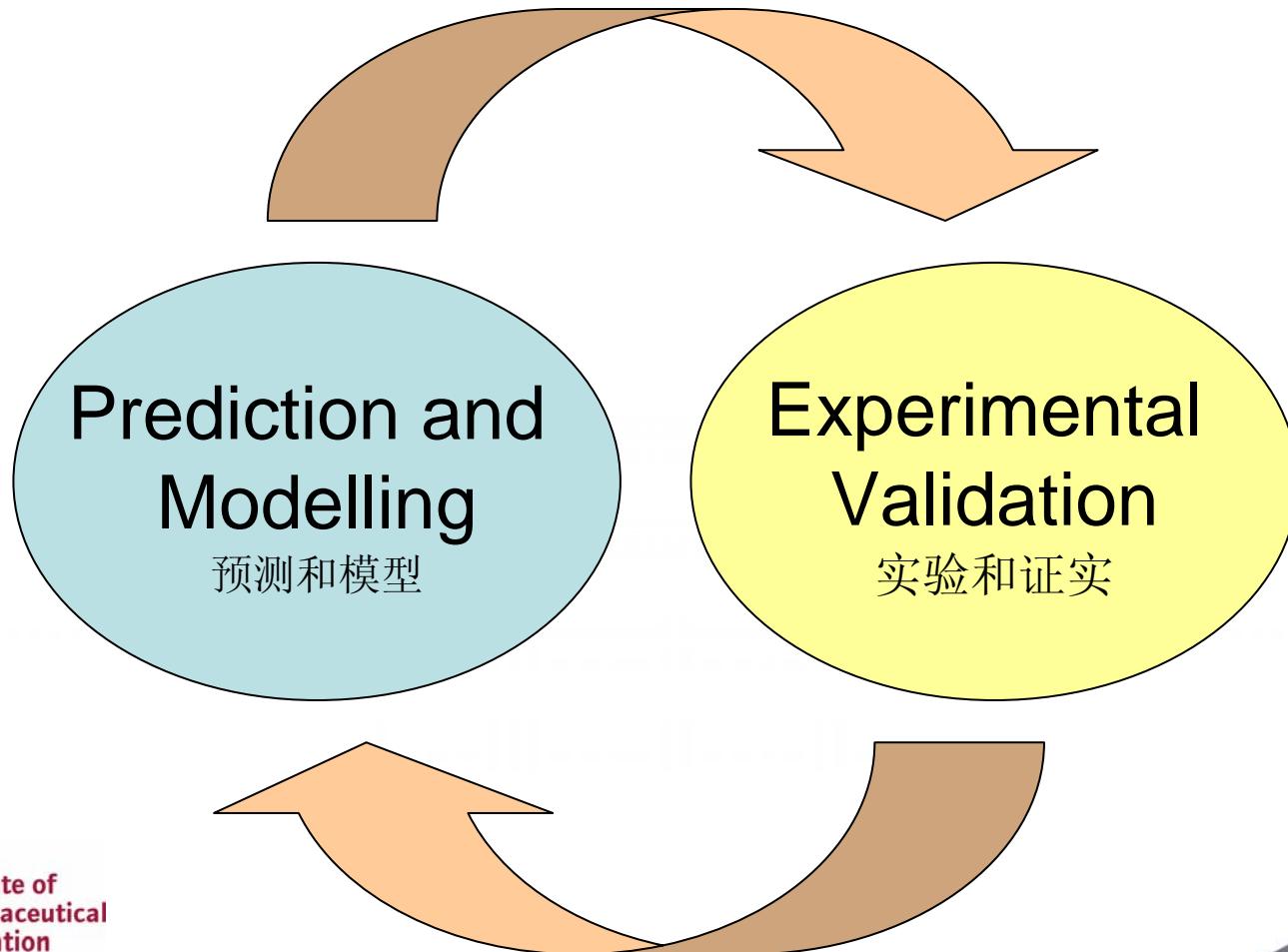
- **Pharmaceutical Formulation** 医药制剂
  - Innovative approaches for new product development
  - prototype formulation, reformulation
- **Pharmaceutical Analysis** 药物分析
  - New method development
  - Product evaluation
  - Product development support
- **Product and Technology commercialisation**  
产品和技术的商业化
  - New companies : Own technology (Spin-out)
  - New companies : 3<sup>rd</sup> party technology (Spin-in)
  - A base in Europe



some of the companies we are working with...

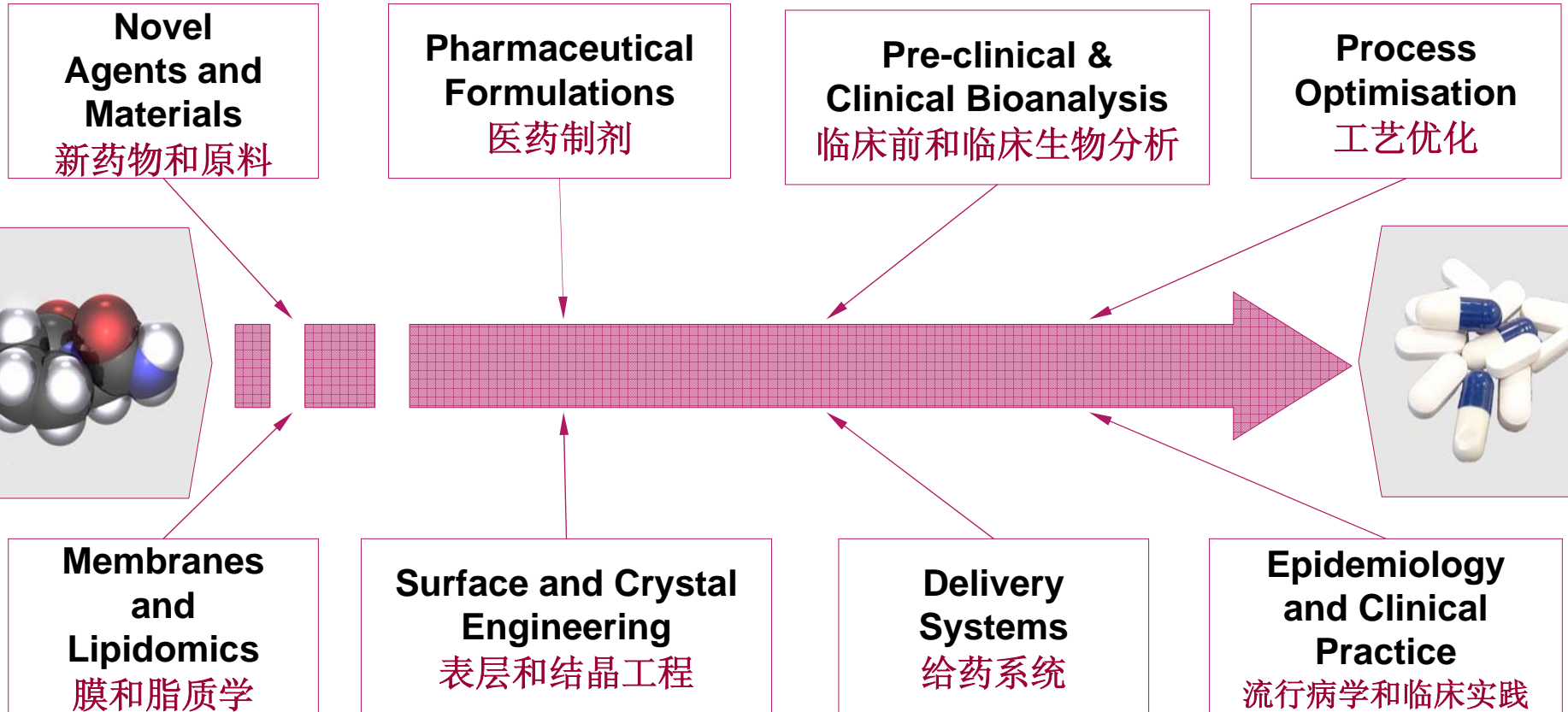
# IPI Research Principle

## IPI 研究原则





...predict success  
...anticipate failure  
...accelerate drug development



Underpinned by Novel/Enhanced Analytical Tools

# Priority research projects

- Pulmonary delivery 肺部给药
- Nanotherapeutics 纳米医疗
- Crystal Engineering
- Formulating Poorly soluble drugs
- Knowledge engineering to link formulation and device characteristics with patient clinical outcomes  
应用知识工程技术建立药剂，给药装置和对病人的疗效之间的关系
- T(C)M Modernisation 传统(中)医药的现代化
- Protein formulation/crystallisation 蛋白制剂 / 结晶法
- Specific drug development programmes 对特殊药物的开发方案的设计



## Breaking News on Pharmaceutical Technology

### Pulmonary drug delivery positioned for growth

**21/04/2006- The groundbreaking approval of Exubera signals that exciting times are ahead for the pulmonary route of drug delivery in many disease areas.**

Many drugs, such as hormones, that are currently used to treat a range of chronic diseases, can only be given by injection and an effective alternative delivery method will be welcomed in many patient groups.

The January approval of Exubera is the first time that a drug has been approved using pulmonary delivery to treat a systemic disease and the decision now opens the door for this delivery method to be used in wider disease applications.

*"In the current climate, it is tough to get new drugs approved, particularly inhalation products, due to the limitations of this route,"* said Leslie Williams, an inhalation technology expert and president & CEO of the specialist pulmonary inhalation technology company Ventaira.

*"One can't underestimate the opportunity this presents for new treatments to be developed that can be delivered by the lungs to treat diseases that are not related to the lungs,"* she told **In-PharmaTechnologist.com**.

The pulmonary drug delivery market is currently worth \$13bn (€10.5bn) and is tipped to grow to \$25bn over the next decade as it encompasses new therapeutic areas, with diabetes playing a large part of that growth.

Other budding therapeutic areas include multiple sclerosis (MS) and certain antibiotics and antivirals.

The approval is set to spark revival in the drug reformulation business, which had been growing steadily between 2000-03 but has since slowed down.

One company working in this area is Ventaira, focused on finding novel formulations of existing off-patent compounds that can be delivered by the pulmonary route to treat chronic diseases.

Later this year, Ventaira will begin Phase II trials with its new inhalation device and formulation of a steroid for asthma/COPD called Mystic.

According to Williams, the device will deliver the drug in a consistent dose with 80 per cent accuracy, compared to current devices that are inefficient in delivering an adequate dose, with only 10 to 15 per cent of the drug getting into the lungs.

*"Reformulation is an area that many big pharma companies are now looking at as a way to manage the lifecycle of existing blockbuster drugs,"* said Williams.

*"There is enough room for all of us in this space, as there is no one drug delivery device that does everything,"* she said.



# Pulmonary Delivery

- Recent launch of Exubera (inhaled insulin) is an important precedent  
最近上市的Exubera（吸入胰岛素）是一个重要的里程碑
- Potential for other pharmaceutical / biopharmaceutical agents to be given in inhaled form  
预示着其他化学和生物药的吸入给药的可能性
- Particle engineering (supercritical fluids, co-crystals for combination therapy, micro emulsions)  
微粒工程（超临界技术，共结晶以产生联合疗效，微乳液）
- Novel inhaler and nebuliser design  
新颖吸入器和喷雾器的设计
- Exploring relationship between patient use and product/device characteristics  
探索病人使用的效果和产品 / 装置的特点之间的关系

# Nanotherapeutics

- **Generating therapeutic nanoparticles** 制造医疗用纳米颗粒
  - High turbulence nano-milling 高湍流的纳米碾磨
  - Microfluidics 微射流技术
  - Supercritical fluids 超临界技术
  - Sonication etc 超声波降解法等等
- **Engineering co-crystals and 'stealth particles'**  
设计制造共结晶和 '隐密微粒'
- **Understanding nanotherapeutics** 了解纳米医疗
  - Targeting at cellular level 靶向细胞级别
  - Dissolution, bioavailability 溶出度, 生物利用率
  - Toxicity 毒性



# Crystal Engineering

- Nanoparticle production
- Crystal structure prediction
- Particle formation using Supercritical fluid technology (SCF)
- Co-crystallisation and epitaxy
- Habit and surface modification
- Polymorph control and selection



# Formulating poorly soluble drug

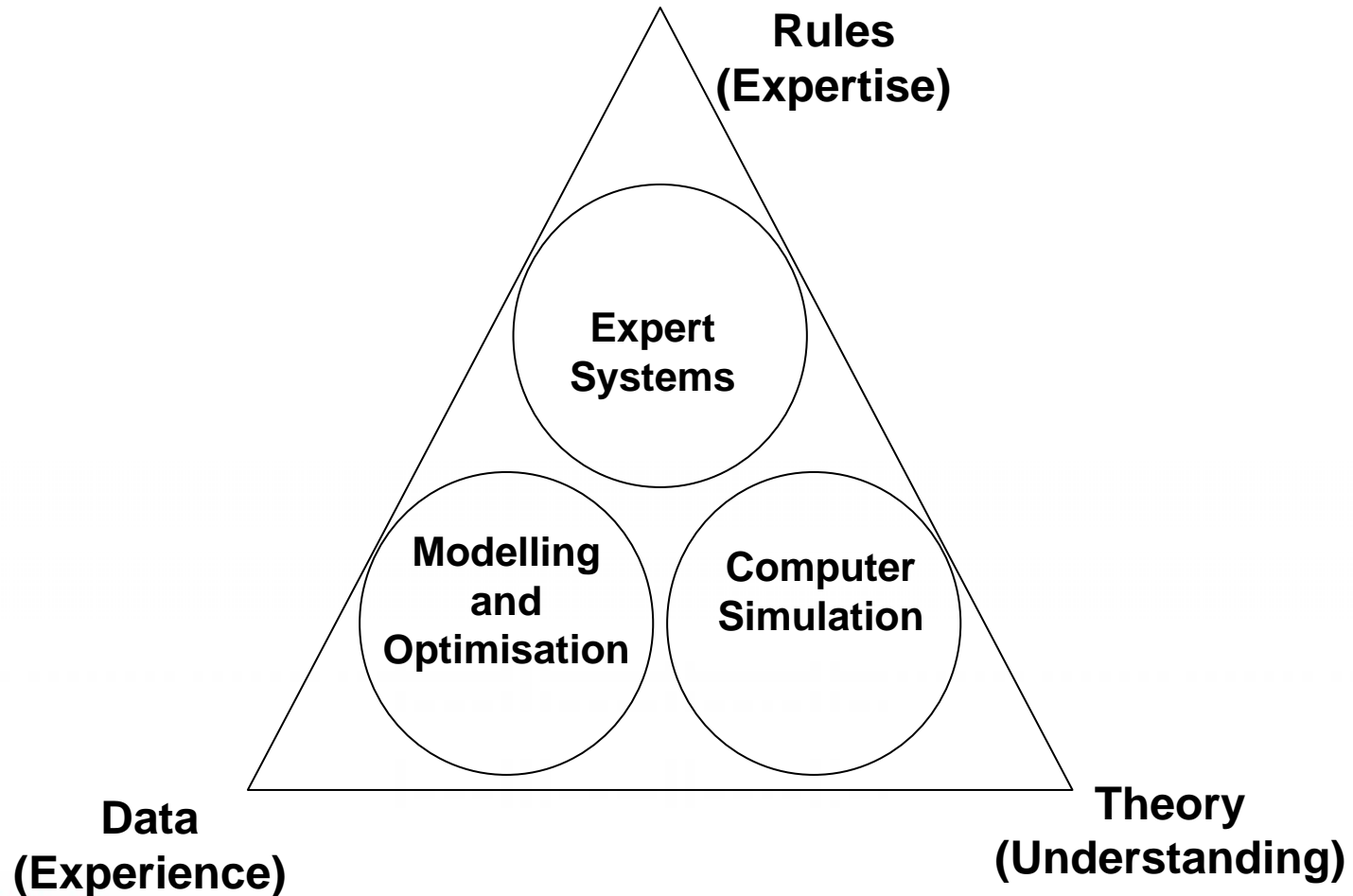
- New technology for nanosuspension formation
- Stabilisation of amorphous materials
- Co-crystal formation
- Complexation and lipidic dosage forms



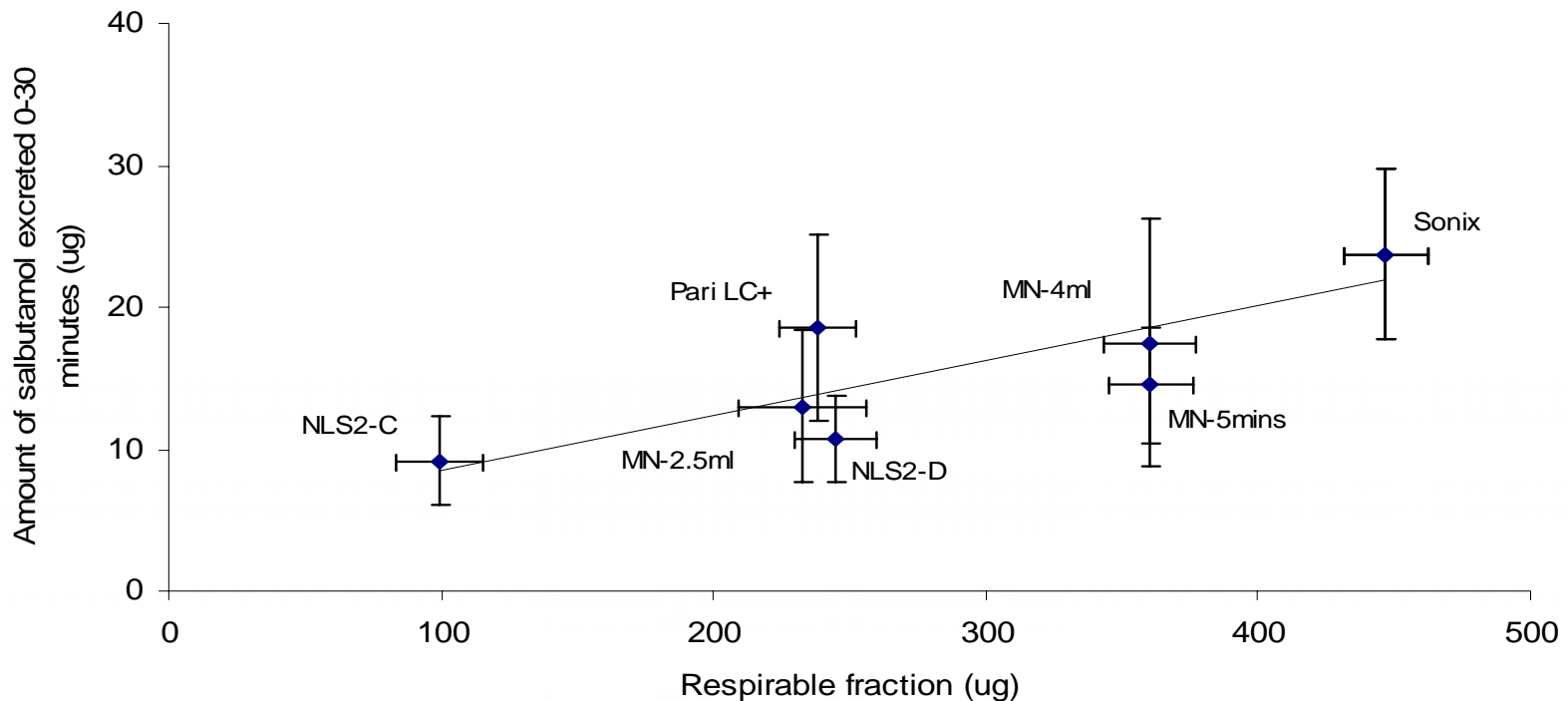
# Knowledge Engineering to link drug and device with patient outcomes

- Current approaches to formulation are highly empirical  
当前的制剂方法非常依赖经验
- Differing patient responses to drugs accepted as the norm  
在制剂设计中区分不同病人对药物的不同反应已被接受为规范
- Links between product variability (e.g. particle size), device performance (e.g. inhaler), patient compliance and (patient-specific) clinical outcomes have traditionally not been well-understood  
传统的方法无法将产品差异（例如，颗粒度），装置的性能（例如，吸入器），病人的配合和（特定病人群体）临床疗效之间的因果关系
- Data-mining (artificial intelligence) technology applied in the IPI are finding important new knowledge  
IPI应用的数据采掘（人工智能）技术在寻找重要的新知识

# INTEGRATION IS THE KEY - THE KNOWLEDGE TRIANGLE



# IVIVC for inhalation therapy

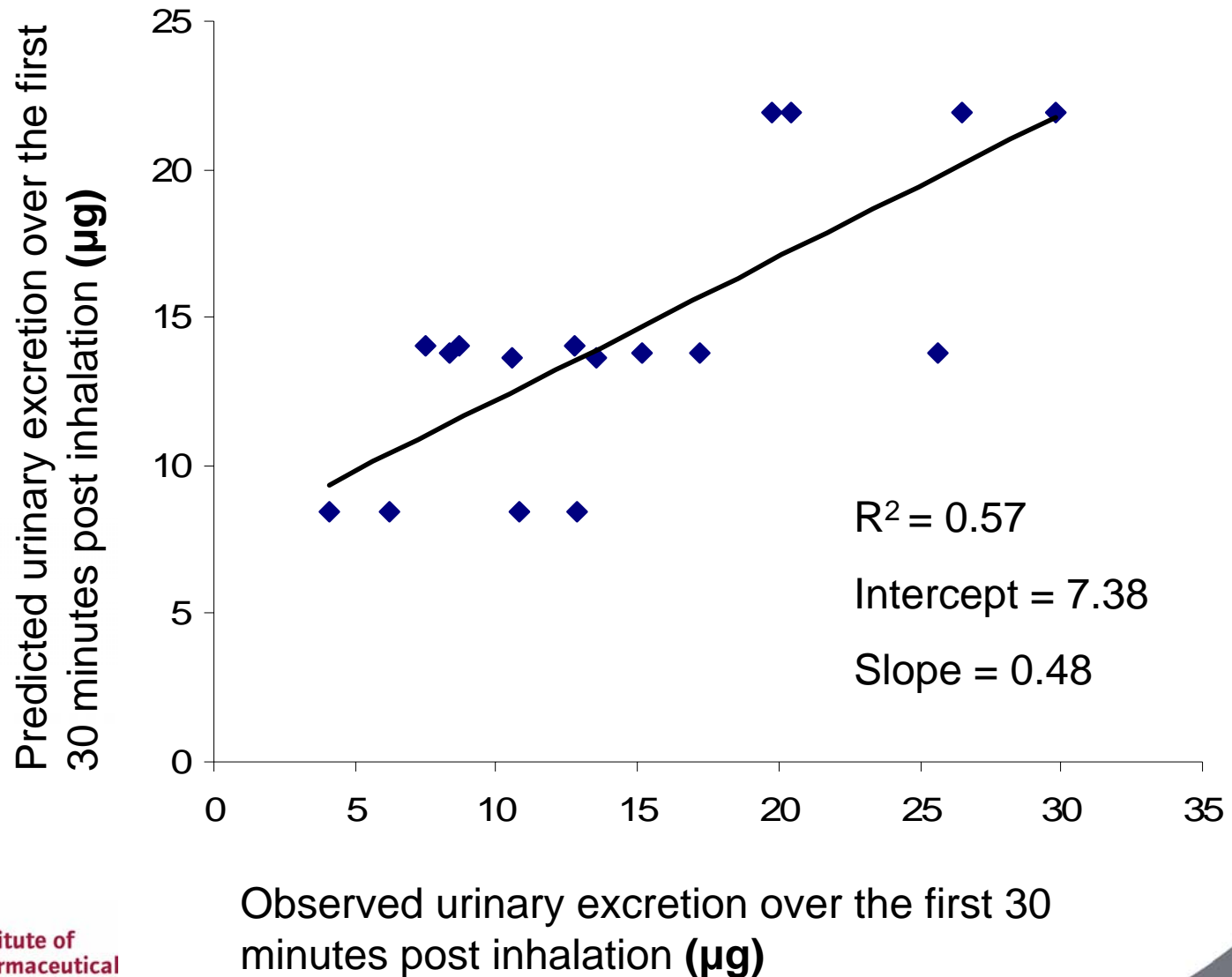


General trends observed but full understanding of all causes of variability and factors affecting in-vivo performance not fully defined

**Table 2 The list of variables evaluated using ANNs and associated data ranges**

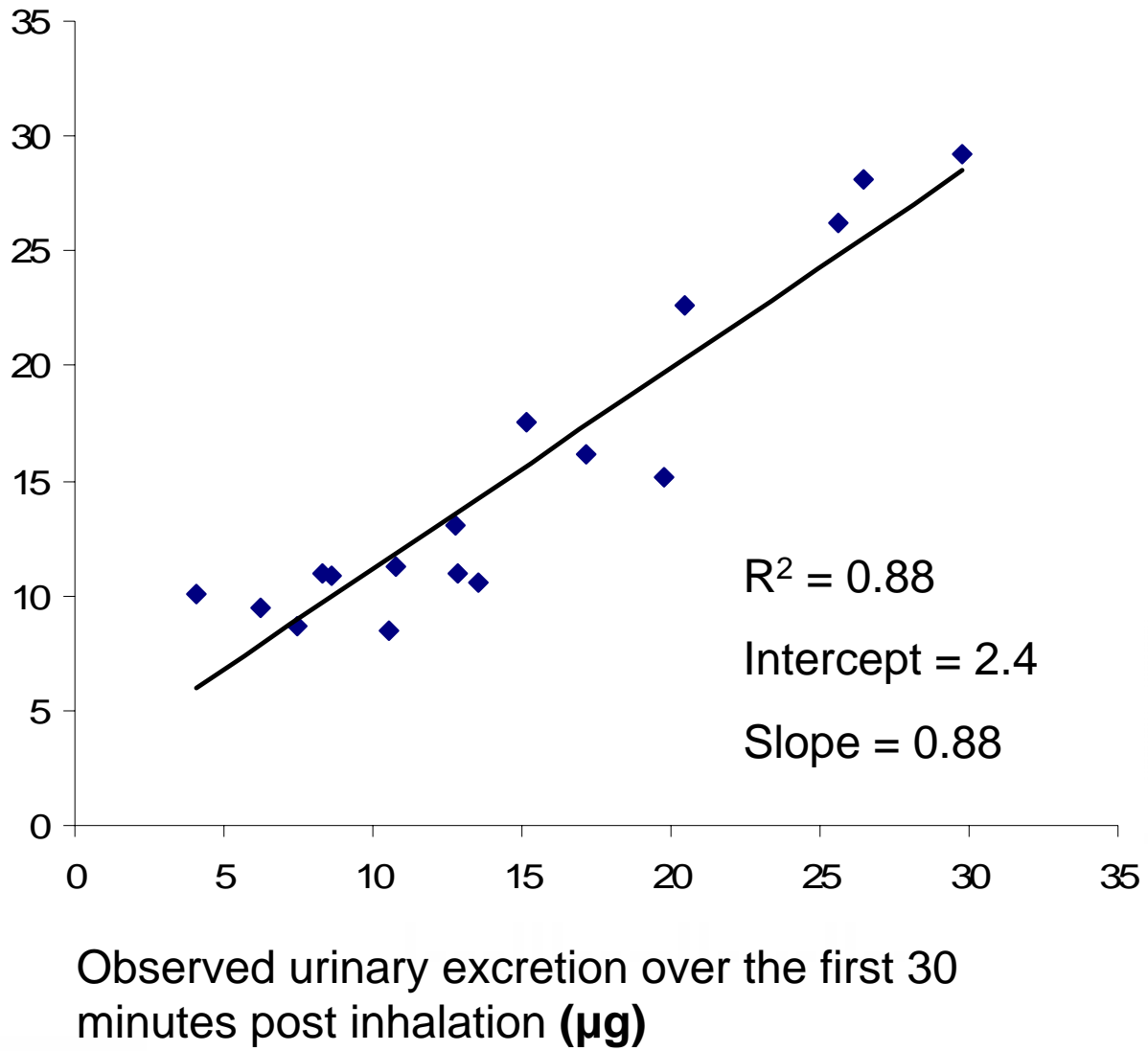
<b>Variables</b>	<b>The data range</b>
<b>Gender</b>	<b>F, M</b>
<b>Age (years)</b>	<b>24 – 55</b>
<b>Body surface area (m<sup>2</sup>)</b>	<b>1.69 – 2.23</b>
<b>Amount of particles in size range 14.8 – 21.8 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>3.5 – 32.8</b>
<b>Amount of particles in size range 9.8 – 14.8 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>11.6 – 87.8</b>
<b>Amount of particles in size range 6 – 9.8 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>39.9 – 97.3</b>
<b>Amount of particles in size range 3.5 – 6 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>42.2 – 250.4</b>
<b>Amount of particles in size range 1.55 – 3.5 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>34.2 – 170.1</b>
<b>Amount of particles in size range 0.93 – 1.55 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>9.6 – 37.4</b>
<b>Amount of particles in size range 0.52 – 0.93 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>4.8 – 37.7</b>
<b>Amount of particles in size range less than 0.52 <math>\mu</math> m inhaled (<math>\mu</math> g)</b>	<b>2 – 15.5</b>
<b>Breath-enhancement</b>	<b>Yes (1)/No (0)</b>
<b>Mode of nebulization</b>	<b>Constant(0)/Dosimetric (1)</b>
<b>Urinary salbutamol excreted at 30 minutes post inhalation (<math>\mu</math> g)</b>	<b>4.1 -35.3</b>

## Statistic modelling approach



# Artificial neural network approach

Predicted urinary excretion over the first 30 minutes post inhalation ( $\mu\text{g}$ )



# Traditional Medicines

- Knowledge engineering tools provide 知识工程手段
  - means of understanding relevance of actives, excipients and 'impurities'
  - Insight into links between therapy and clinical effect
- World class analytical facilities 世界级分析设施
  - Molecular and structural characterisation
  - Separation science
  - Bioanalysis
- Providing regulatory advice to MHRA Chemistry and Pharmacy standards 向MHRA提供有关化工和制药法规方面的建议
- Research project examples include China TCM Metabonomics; Apiceuticals



# Crystallisation of proteins in Drug Delivery

- Regulatory approvals of biological agents now exceeding those for small molecules

获批的生物制剂已经超过了小分子药物

- Many proteins/large molecules are only available in injectable form

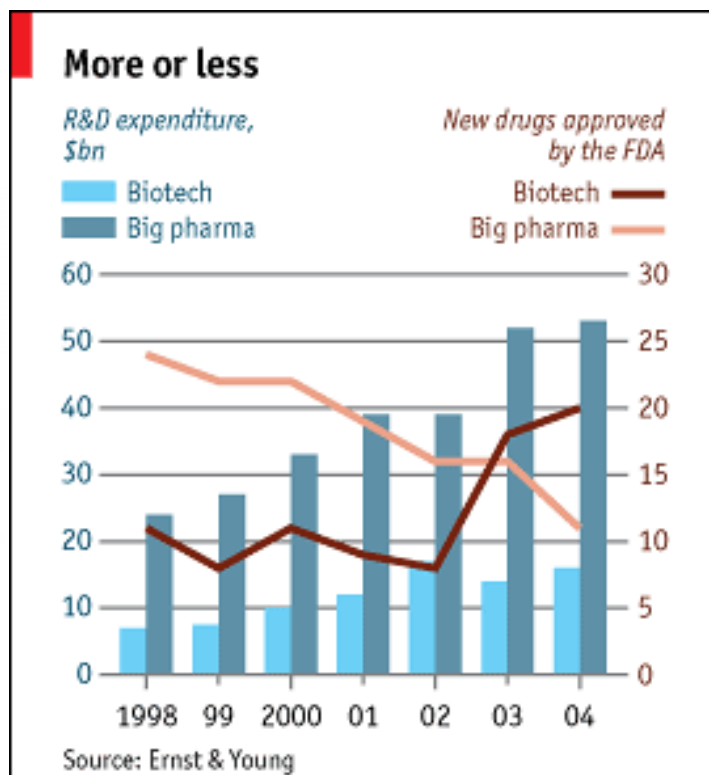
很多蛋白/大分子只能通过注射给药

- Particular stability/handling/processing issues

稳定性/操作性/工艺问题

- Ongoing research to develop stable crystal forms and alternative formulations

开发稳定的晶型和其他的剂型的研究正在进行中



# Specific Drug Development programmes

- Humanised monoclonal antibody as potential anti-cancer and anti-thrombosis agent
- Antibody acting on beta-1-integrin showing promise in reversing emphysema, rheumatoid arthritis
- Institute of Cancer Therapeutics – now open





# China business strategy (1)

- Science exchange through collaborative research, PhD programmes etc 通过科研合作和博士项目等实现学术交流
  - e.g. Therapeutic nanoparticles; in-silico formulation; Quality by Design
- Providing advice to Chinese companies on regulatory compliance, formulation design, manufacturing optimisation 向中国企业提供法规咨询，制剂设计，以及生产优化的服务
- Business development partnerships, where possible using scientists and facilities in China 建立商业合作伙伴关系，尽可能地使用中国国内的科研资源



# China business strategy (2)

- Helping Chinese companies and entrepreneurs to exploit novel technology in global healthcare markets  
帮助中国企业和企业家开发面向全球市场的新技术
- Strategic research partnerships (e.g. CNANE)  
战略合作伙伴 (例如, 纳米工程院)
- Licensing and commercialisation of technology into Chinese markets  
在中国市场上进行技术的商业化
- New joint venture companies 建立合资公司



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## In summary...

- IPI technology, expertise and experience of global markets  
IPI的技术，专长，和全球市场经验
- Extensive opportunities for Chinese companies, institutes and inventors  
对于中国企业和研究机构存在广阔的机会
- Specific capabilities in the IPI in pharmaceutical formulation, product development, technology commercialisation  
IPI专注于制剂开发，新产品开发，和技术的商业化
- We are keen to work with you!  
我们很希望与您合作！



**Thank you for  
listening**