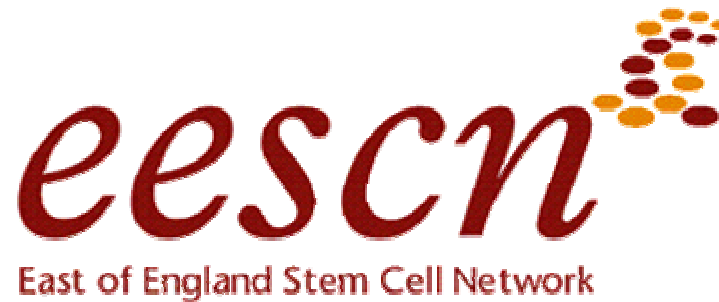


*Investing in stem cells: a venture capital perspective*

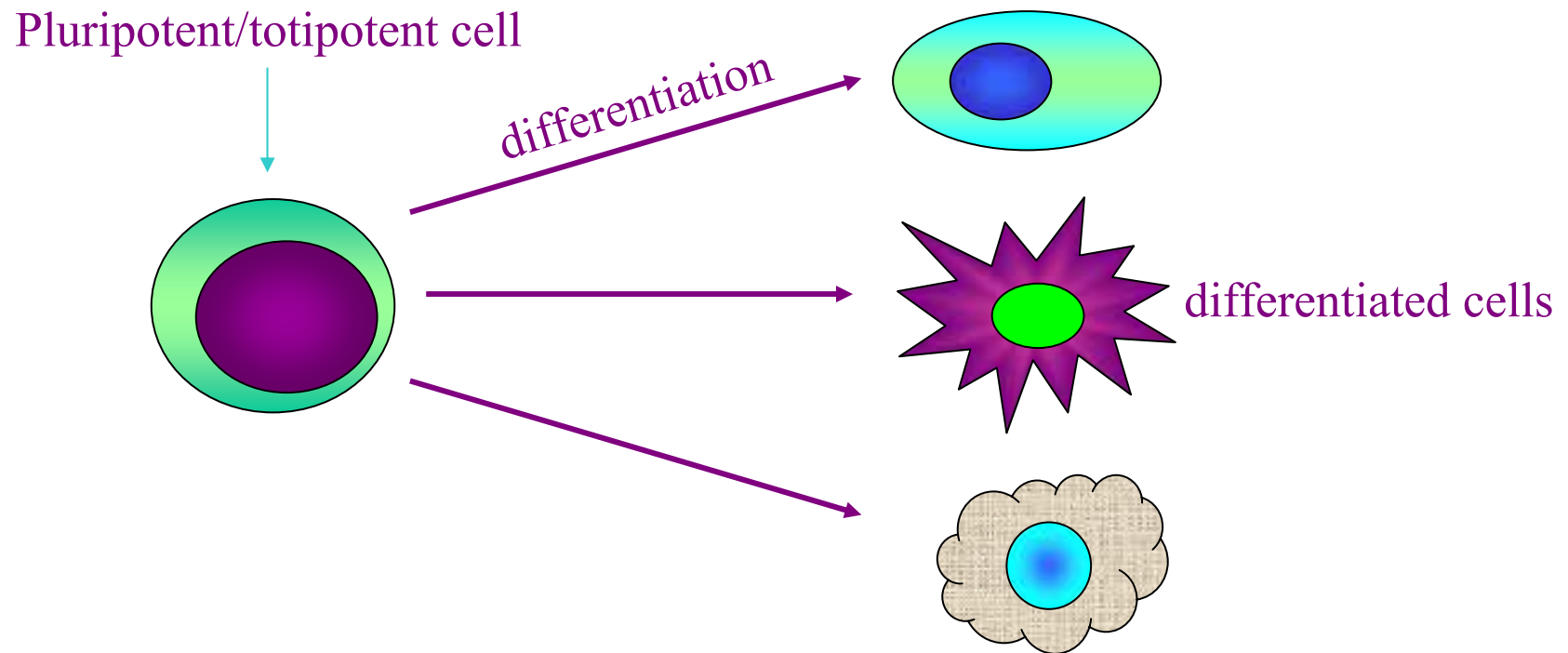


8<sup>th</sup> March 2005

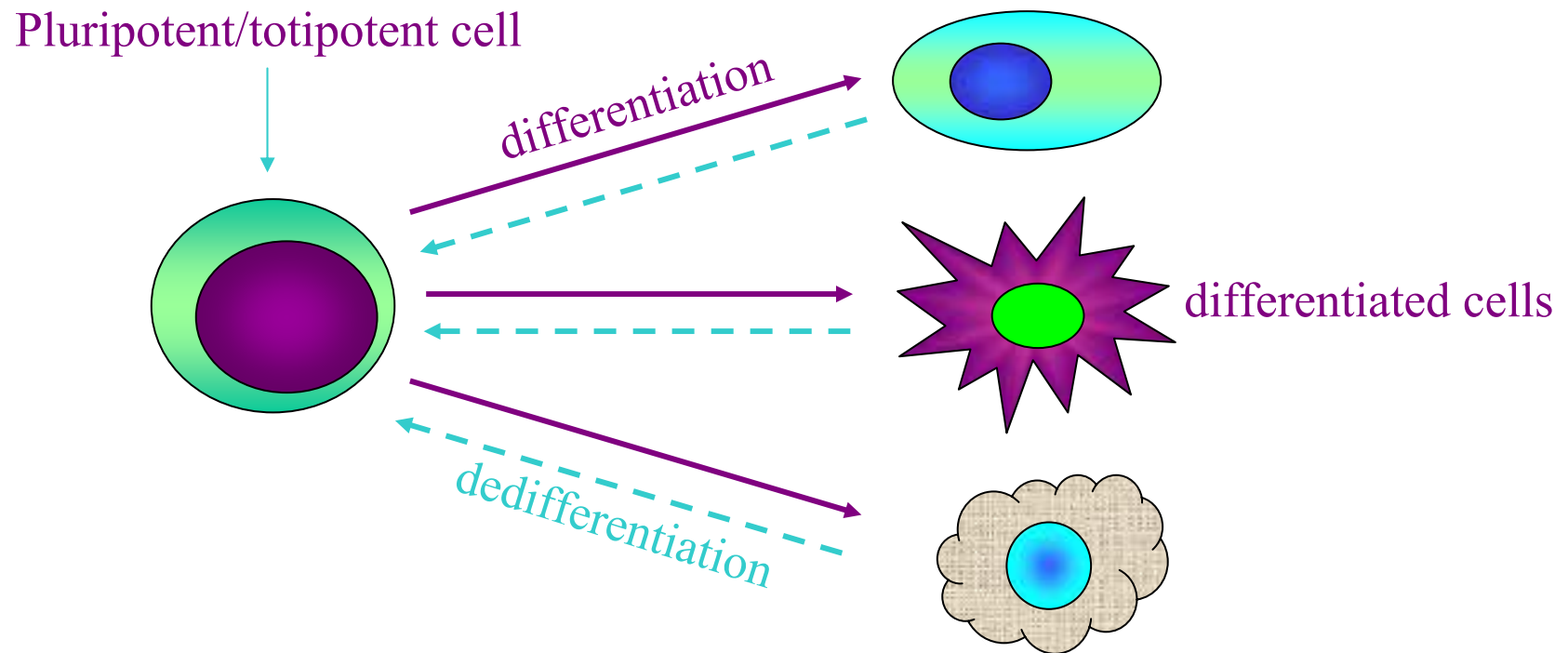
**Dr. Cathy Prescott**  
Science Director  
Avlar BioVentures Ltd

Avlar BioVentures Ltd.  
Highfield Court  
Church lane  
Madingley, Cambs  
CB3 8AG  
Tel: +44 (0) 1954 211 515  
[www.avlar.com](http://www.avlar.com)

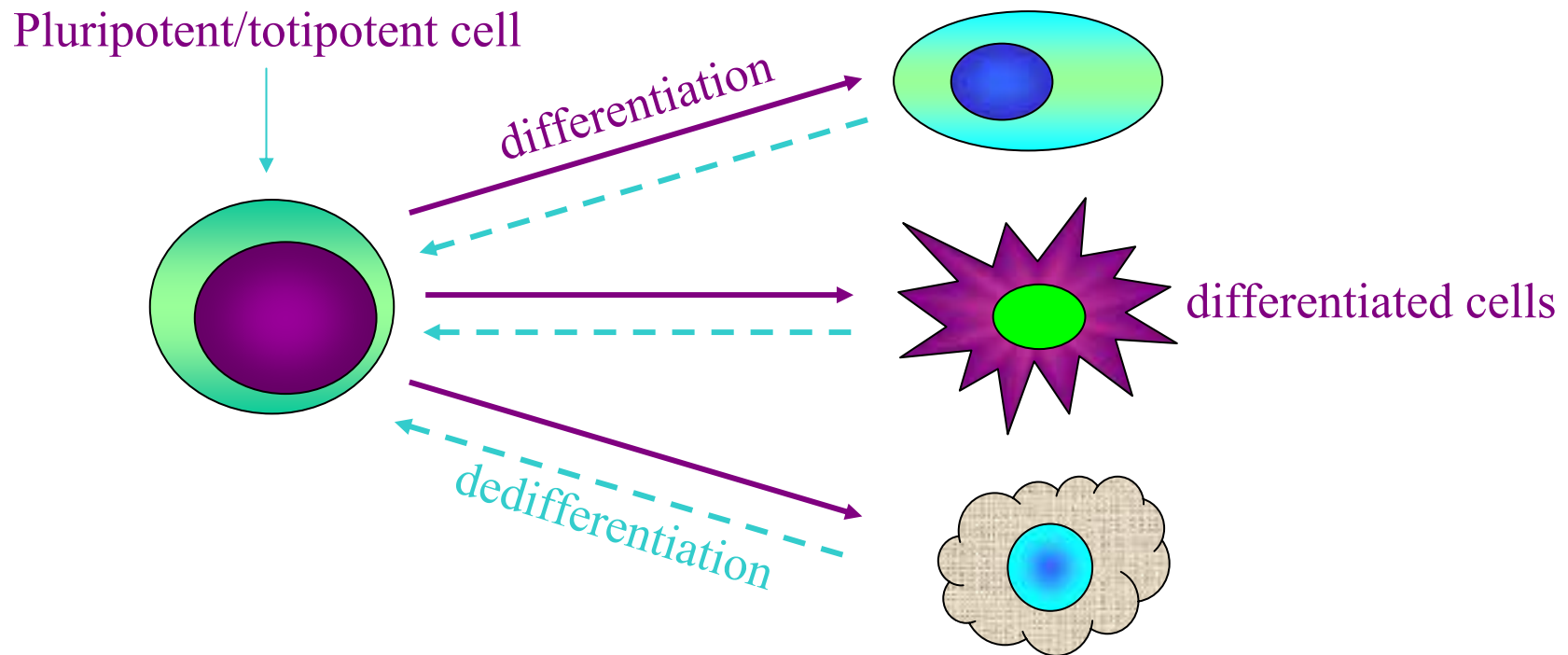
# *The plasticity of cells*



# The plasticity of cells



# The plasticity of cells



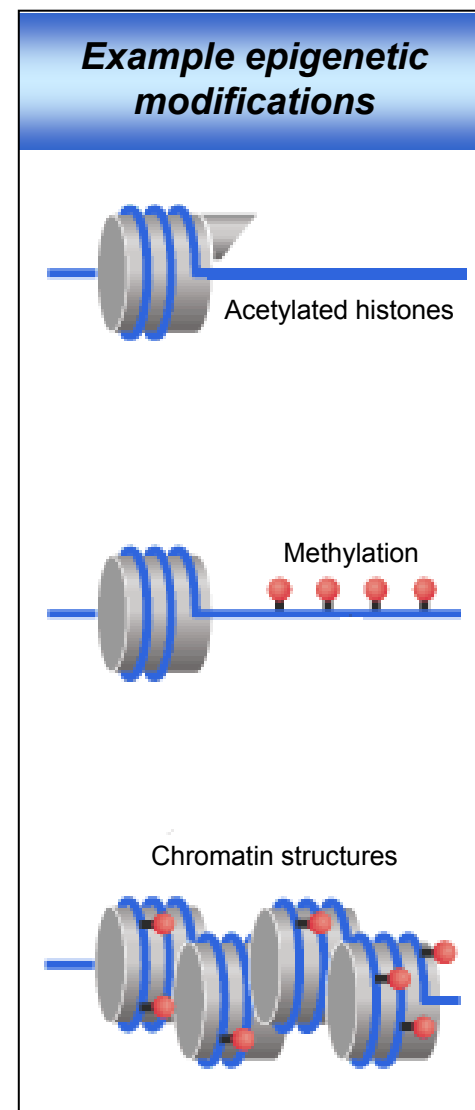
*How can cells with the same DNA content, have different functions?*

# Epigenetics governs cell fate

Different types of cells have widely differing functions but contain the same set of genes

Differences are due to which genes are turned on or off

The selective control is governed by functional groups which sit on top of the genes: *epi-genetics*



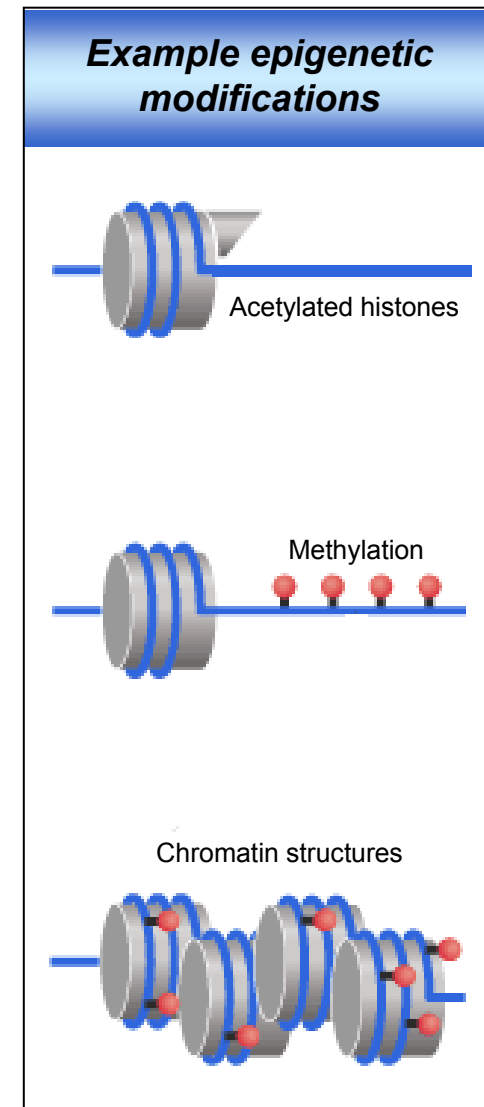
# Epigenetics governs cell fate

Different types of cells have widely differing functions but contain the same set of genes

Differences are due to which genes are turned on or off

The selective control is governed by functional groups which sit on top of the genes: *epi-genetics*

*How is the epigenetic status of a cell regulated?*



# *The value of understanding epigenetics*

Mechanistic knowledge of epigenetics  
& the factors involved



Control of cell fate



Potential applications



Cell-based  
therapy

Other  
applications?

*From a venture perspective:*

---



1. What will it take to get stem cell-based products into patients?
2. How else can our knowledge of cell fate be exploited?

*From a venture perspective:*



1. What will it take to get stem cell-based products into patients?

Status of Research

Regulatory Position

Clinical Impact

Commercial Models

Patent Policy

## CURRENT STATUS

## IMPACT

Early Stage

Long term commitment to R&D  
Funding fundamental (vs. applied) research  
Lengthy-timelines to reach commercial product

Focus

Control of cell behaviour, proliferation & stability  
Cell source – embryonic versus adult stem cells

Disease models

Development, relevance, delivery, timing ....  
E.g. will dopaminergic cells alone cure PD?

# Regulatory



## CURRENT STATUS

National rules apply

Evolving framework

## IMPACT

Multiple clinical trials  
Increased costs/ lower margins  
Fragmented (smaller) markets  
Difficult to partner

Complexity of harmonising European regulation led to recent failure of Tissue Engineering Directive  
Risks associated with uncertainty of direction  
Future of animal feeder layers?  
Autologous vs. allogenic therapy?  
QC criteria?  
Implementation of mandatory requirements (time)

## CURRENT STATUS

## IMPACT

Cell-based therapy

Immuno-incompatibility  
Cell source (ethics, risk of teratomas, QC criteria)  
Manufacturing/scale-up (GMP facility & expertise)  
Administration (expertise, storage, ease of handling, stage of delivery)

Big Pharma

Watching - no to cell-based therapy  
Lack of financial, managerial expertise & infra-structure support for clinical trials

Funding clinical trials?

Proposal to establish a UK Stem Cell Foundation  
US federal versus state funding

# Commercial



## CURRENT STATUS

## IMPACT

Business model

Hybrid business model  
Product or service-based proposition?  
Pricing - cure versus management

Market access

Fragmented markets  
Reimbursement status  
(Comparative cost effectiveness vs. conventional approaches?)

Big Pharma

Watching - restricted partner options

US position

Federal versus state support  
CA (\$3Bn), WI (\$375M), NJ (\$9.5M)

**Pharmaceuticals**

High up-front investment

Long development times

High gross margins

Large markets

**Medical Devices**

Lower up-front investment

Short development times

Low gross margins

Focused markets

HYBRID BUSINESS MODEL

**Pharmaceuticals**

High up-front investment

Long development times

High gross margins

Large markets

**Cell Based Products**

High up-front investment

Medium/long development times

Low gross margins

Focused markets

**Medical Devices**

Lower up-front investment

Short development times

Low gross margins

Focused markets

# Commercial



## CURRENT STATUS

## IMPACT

Business model

Hybrid business model  
Product or service-based proposition?  
Pricing - cure versus management

Market access

Fragmented markets  
Reimbursement status  
(Comparative cost effectiveness vs. conventional approaches?)

Big Pharma

Watching - restricted partner options

US position

Federal versus state support  
CA (\$3Bn), WI (\$375M), NJ (\$9.5M)

# Commercial



## CURRENT STATUS

## IMPACT

Business model

Hybrid business model  
Product or service-based proposition?  
Pricing - cure versus management

Market access

Fragmented markets  
Reimbursement status  
(Comparative cost effectiveness vs. conventional approaches?)

Big Pharma

Watching - restricted partner options

US position

Federal versus state support  
CA (\$3Bn), WI (\$375M), NJ (\$9.5M)

Without federal support

“innovation trapped within state borders”

# Patents



---

CURRENT STATUS	IMPACT
Increasing No. patent filings	1990s ~3000 patents granted to biotech companies. 1998 >9000 patents granted to biotech companies. No. patents increasing at a rate of ~25%+/year
European patent convention	Rule 23d(c) provides that uses of human embryos for industrial and commercial purposes are excluded from patentability. Protests & major public debate (e.g. “Edinburgh patent”) Modification of claims
Freedom to operate	Complicated patent position will <i>delay</i> commercial progress

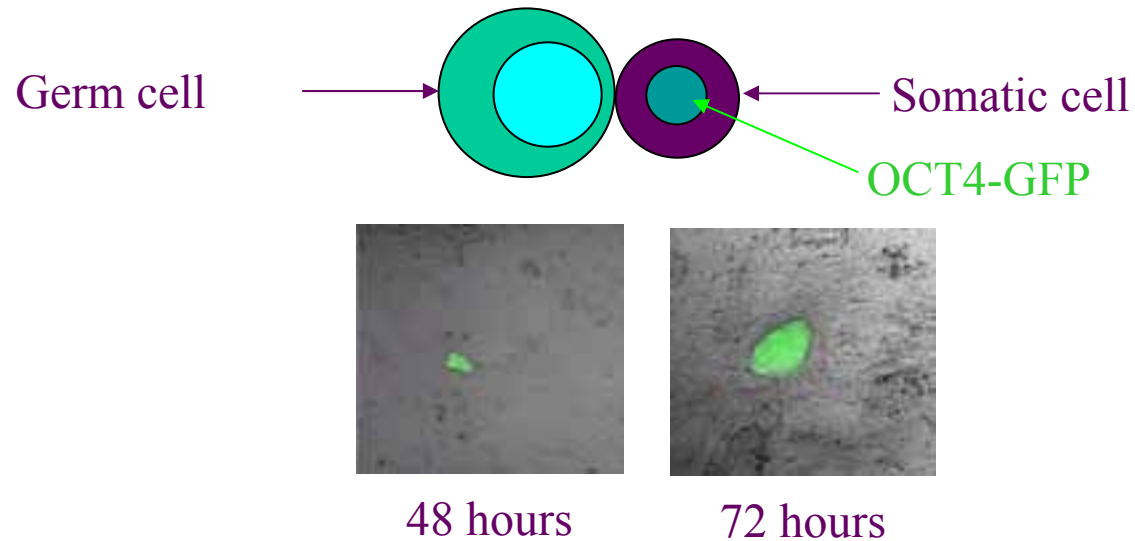
## *From a venture perspective:*

---

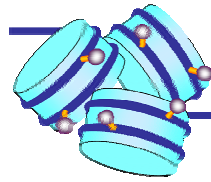


1. What will it take to get stem cell-based products into patients?
2. How else can our knowledge of cell fate be exploited?

# Germ cells contain factors that alter cell fate



Embryonic germ cells induce epigenetic reprogramming of somatic nucleus in hybrid cells. *Tada et al. (1997) EMBO J. 16, 6510*



**CellCentric**

*unlocking epigenetics*

*Avlar*  
BioVentures

Identify epigenetic programming factors, their targets and mimics\*



Control cell fate

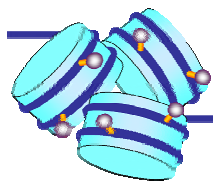
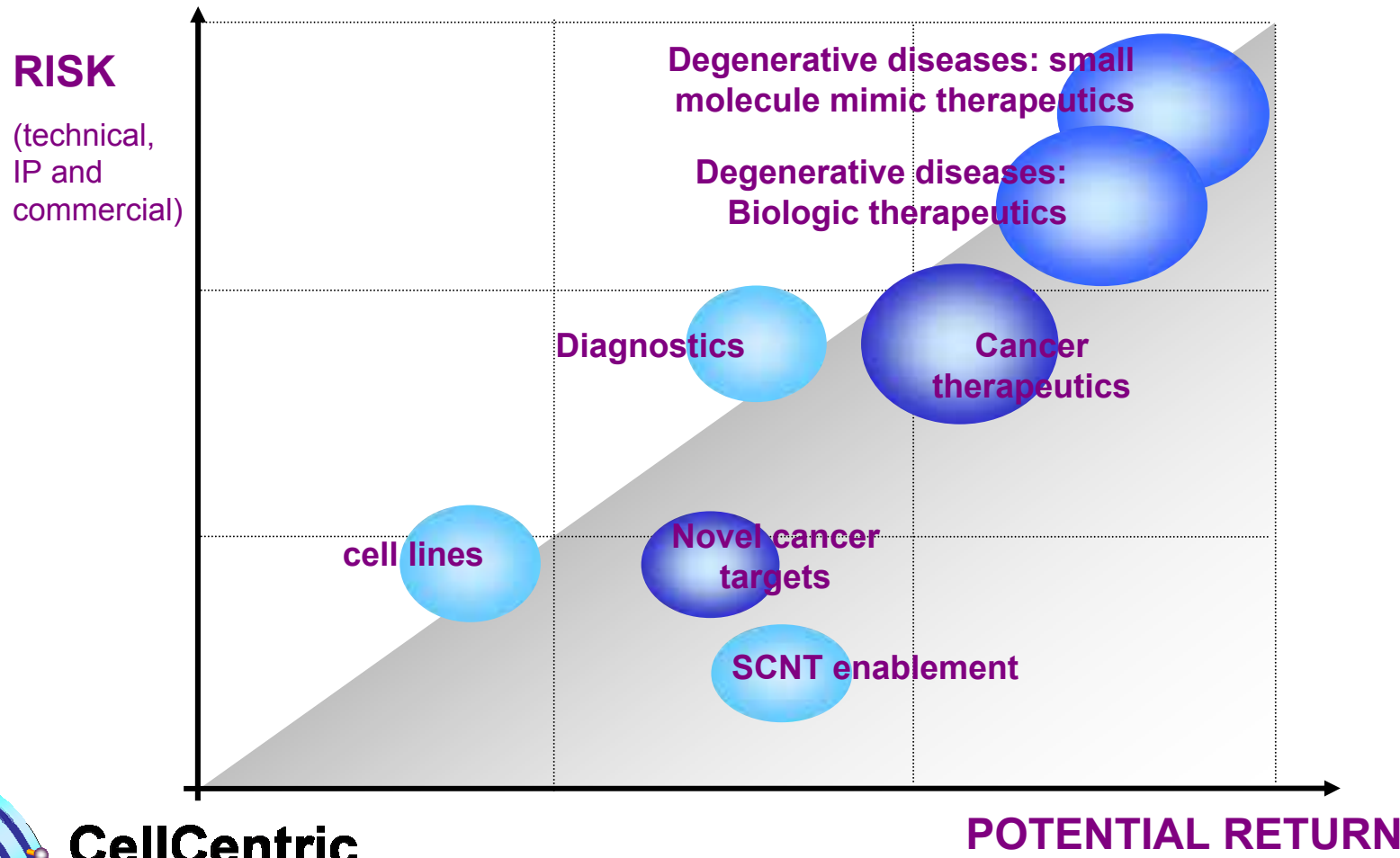


*Applications:*

Clinical & Non-clinical

\*Precedent for small molecule mimics already set “Dedifferentiation of Lineage-Committed Cells by a Small Molecule”. Shuibing Chen et al. (2004) *J. Am. Chem. Soc.*, 126: 410-411.

# What are the applications?



**CellCentric**

*unlocking epigenetics*

# Why epigenetic programming factors?



## RESEARCH

Mechanistic approach to identify the factors that control cell fate

## REGULATORY

Drug-like therapeutics  
Many clear precedents

## CLINICAL

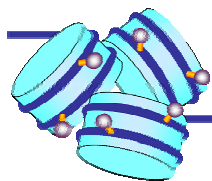
Existing infrastructure & support including manufacturing & delivery

## COMMERICAL

Bridge to pharma & biotech  
Fundable proposition  
Multiple market opportunities both clinical & non-clinical

## PATENTS

Composition of matter



**CellCentric**

*unlocking epigenetics*

*The importance of matching expectations & reality*



---

Exciting new field with huge potential

Notable successes

e.g. use of haematopoietic stem cells for blood disorders

## *The importance of matching expectations & reality*



Exciting new field with huge potential

Notable successes

e.g. use of haematopoietic stem cells for blood disorders

BUT

Imperative at this early stage to get the wider potential right as any clinical setback will undermine confidence in the sector (e.g. Gene therapy, current volatility of pharmaceutical sector)

*“It takes a village to raise a child”*



Success of stem cell ‘therapeutics’ (cell & drug) is dependent on a co-ordinated approach actively engaging all relevant sectors including research, regulatory, clinical, community, ethics, industry & financial

Communication, context & collaboration are all key

Forum to collate information, educate, disseminate & advise

*Albion Innovations*