SCIENCE · TECHNOLOGY · SOCIETY

The University of Nottingham

Innovation challenges in regenerative medicine: some inconvenient truths

Paul Martin
Institute for Science and Society
University of Nottingham

Thanks to …

- ESRC funded project '*Haematopoietic stem cells: the dynamics of expectations in innovation'* with Alison Kraft, Nik Brown and Philip Bath
- EPSRC project on '*User needs in tissue engineering*' with Emma Rowley
  - Martin, P., Hawksley, R. and Turner, A. (2009) *The commercial development of cell therapy – lessons for the future?* ISS, University of Nottingham
  - Rowley, E. and Martin, P. (2009) *Barriers to the commercialisation and utilisation of regenerative medicine*. ISS, University of Nottingham.

SCIENCE · TECHNOLOGY · SOCIETY

Aims

- Expectations and emerging technologies
- Anatomy of the cell therapy industry – firms, products, collaboration
- The problem of clinical adoption
- Dynamics of translation
- Role of social science

SCIENCE · TECHNOLOGY · SOCIETY

The making of a new field

- Stem cells/ regenerative medicine best thought of as a “field in the making”
  - Technical, commercial, clinical and regulatory uncertainty
- Key role of hope and expectations in mobilising resources
- What is the role of social science in making ‘promissory technologies’?
- Resistance to scepticism …

SCIENCE · TECHNOLOGY · SOCIETY

Research undertaken

- Desk based survey of the global cell therapy industry
  - Firm strategies and technologies, products, clinical trials and industry alliances

- Interviews (54) with key stakeholders on barriers to translation (Emma Rowley)

SCIENCE · TECHNOLOGY · SOCIETY

Definitions of cell therapy

- Two types of cell therapy products
  - Primary (contain living cells)
  - Secondary (scaffolds, matrices and biocompatible materials that support tissue repair)
- Two generations of cell-based products
  - First generation products based on non-stem cell therapies, grafts and implants
  - Second generation based on stem cells

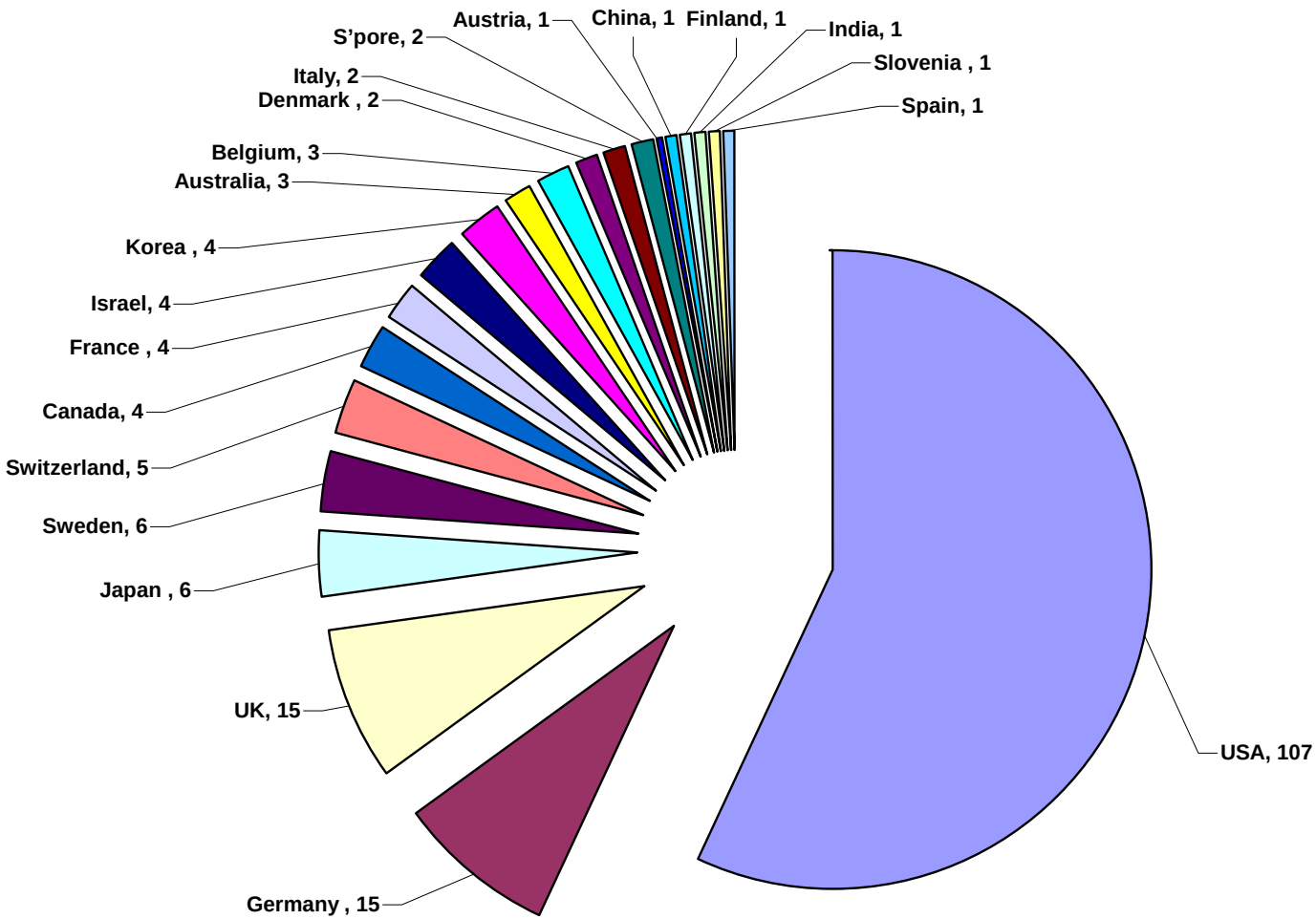
SCIENCE · TECHNOLOGY · SOCIETY

Anatomy of the industry

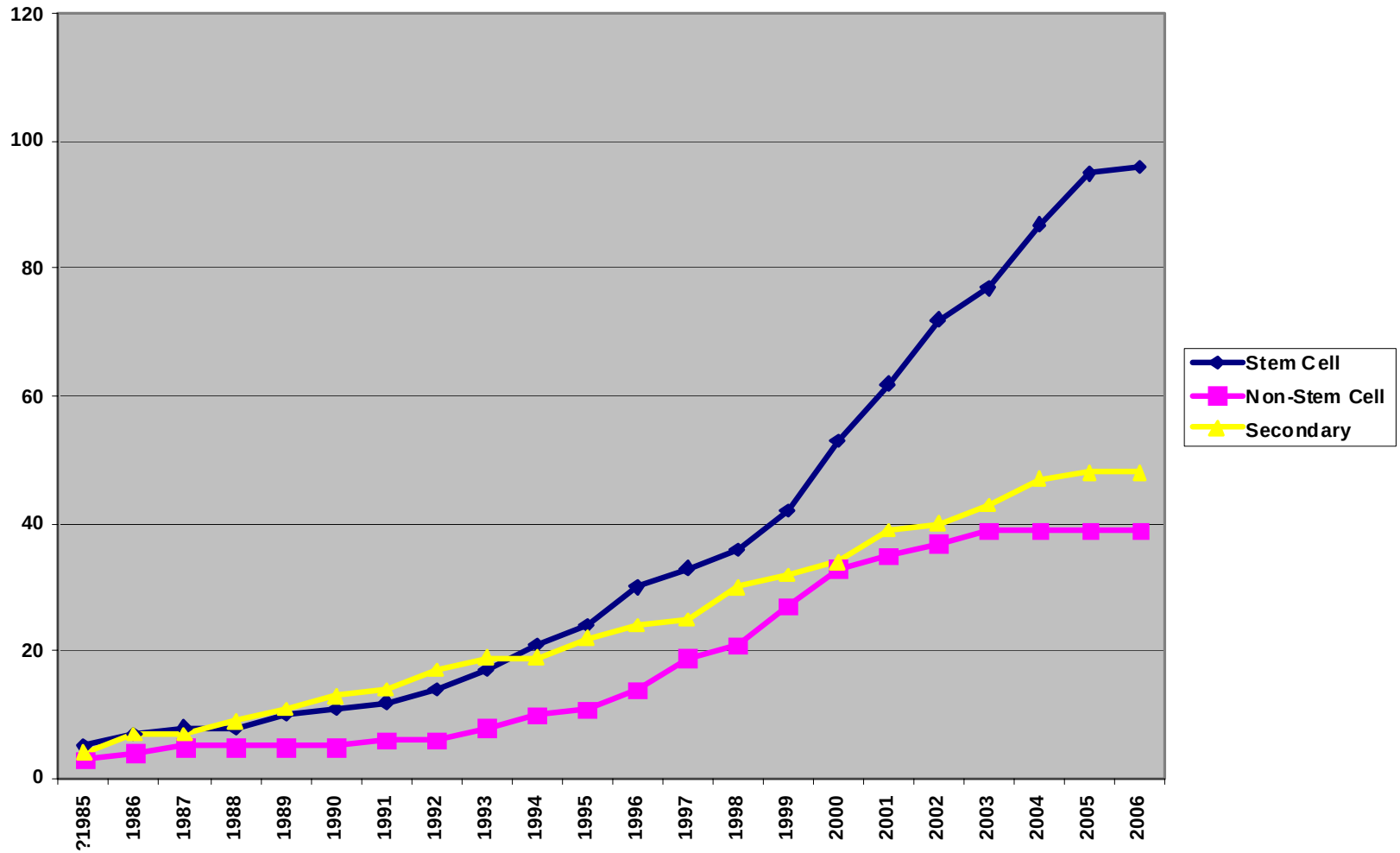
- 187 firms (138 primary + 49 secondary), plus 120 private cord blood banks (not involved in R&D)
- Primary firms are small: 85% <100 staff; only 11 with >500. Secondary firms are larger
- Significant number of primary firms more than 10 years old, with 30% listed on public markets
- Large number with products on market
- But very high level of company failure and problems with firm growth
- International division of labour: US - first generation allogeneic and stem cells; EU - first generation autologous

SCIENCE · TECHNOLOGY · SOCIETY

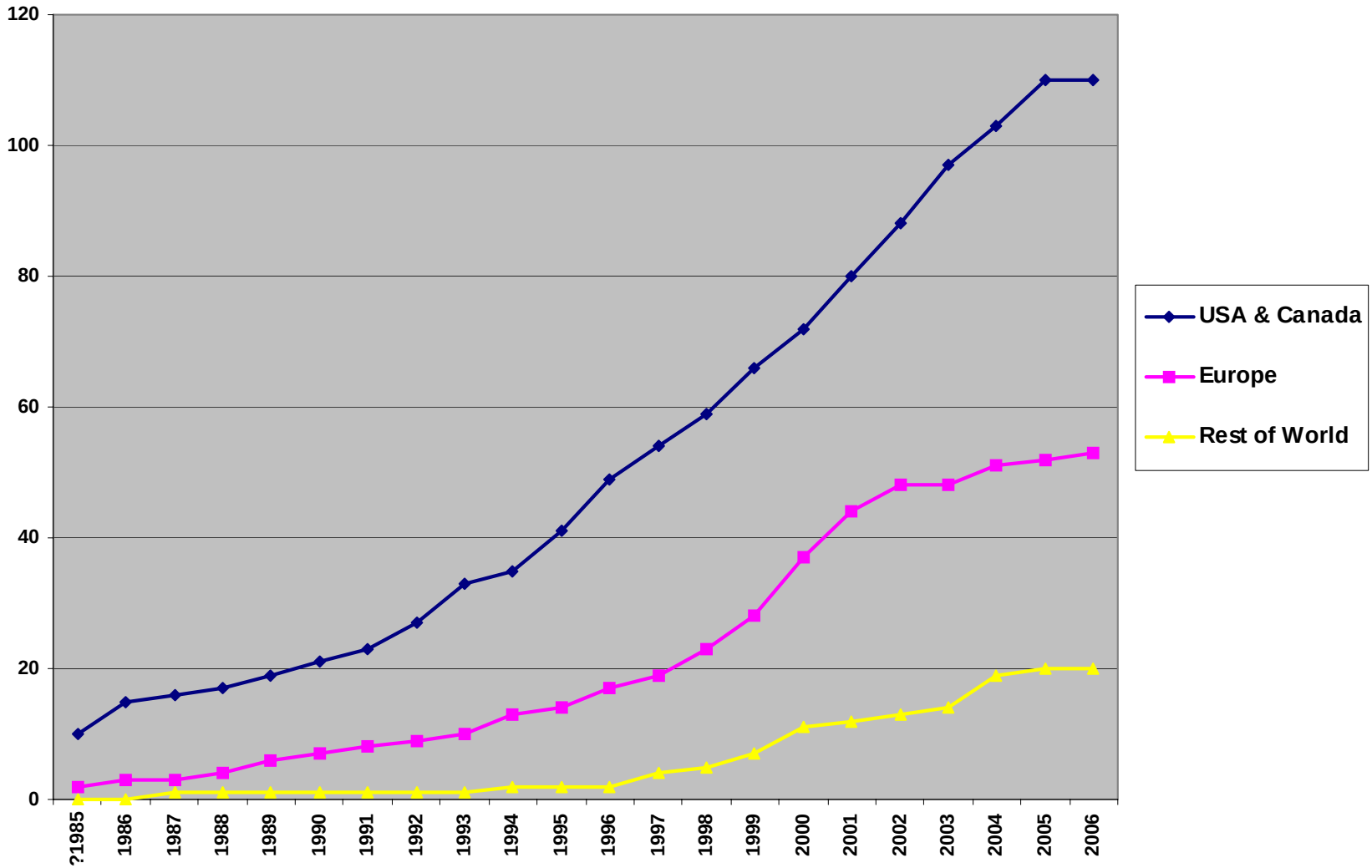
Cell therapy firms by country



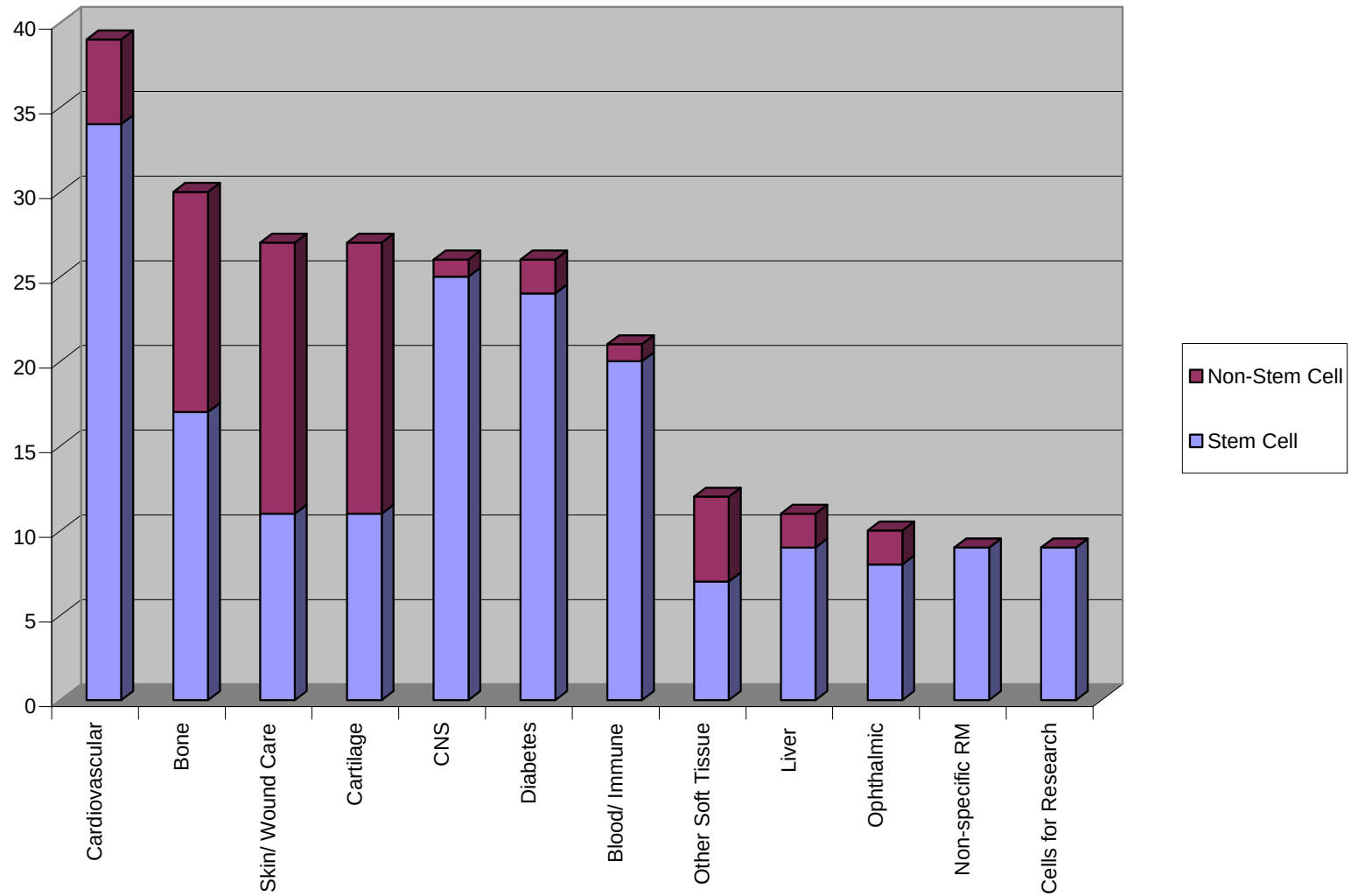
Growth of firms by year founded



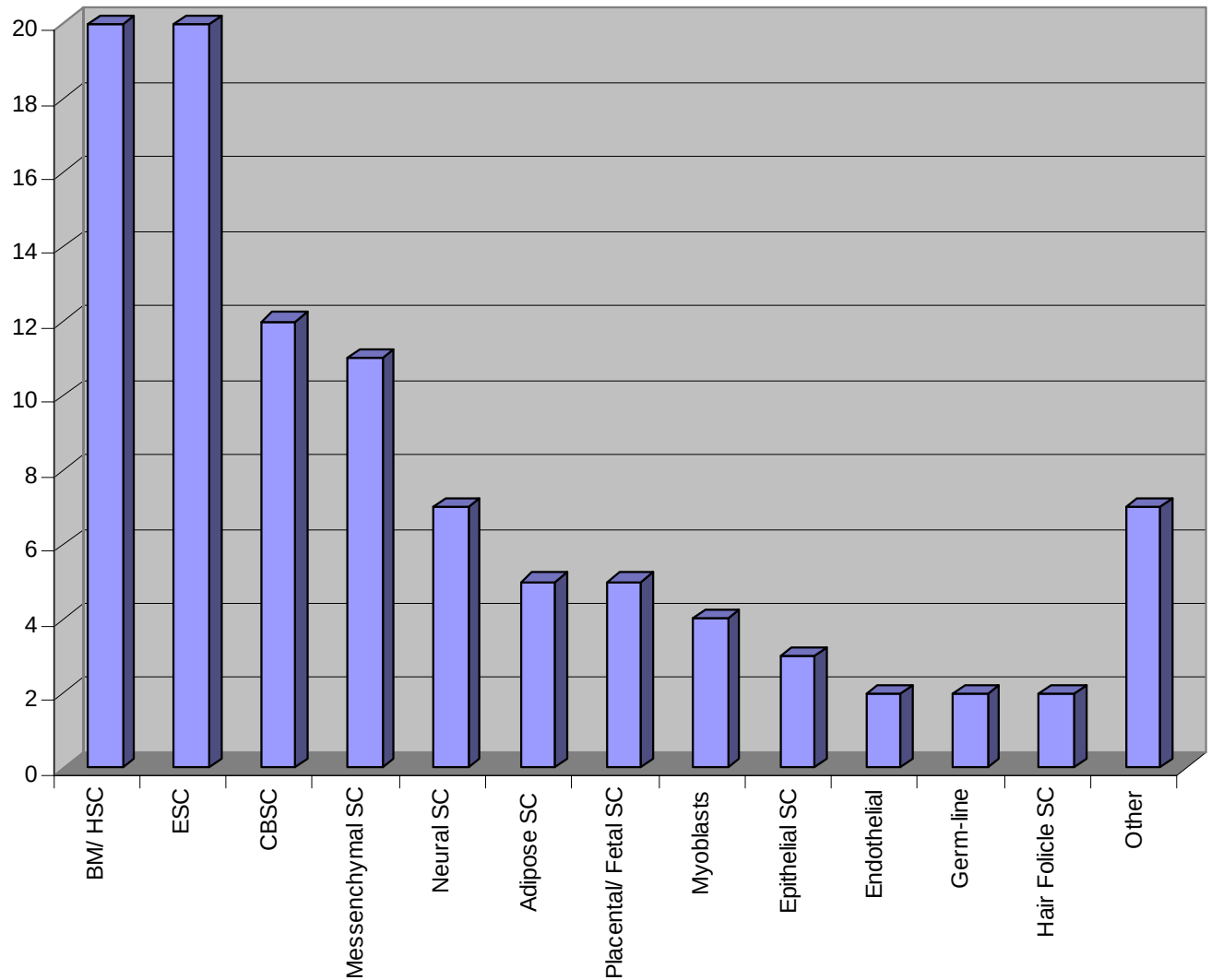
Growth of new firms by location



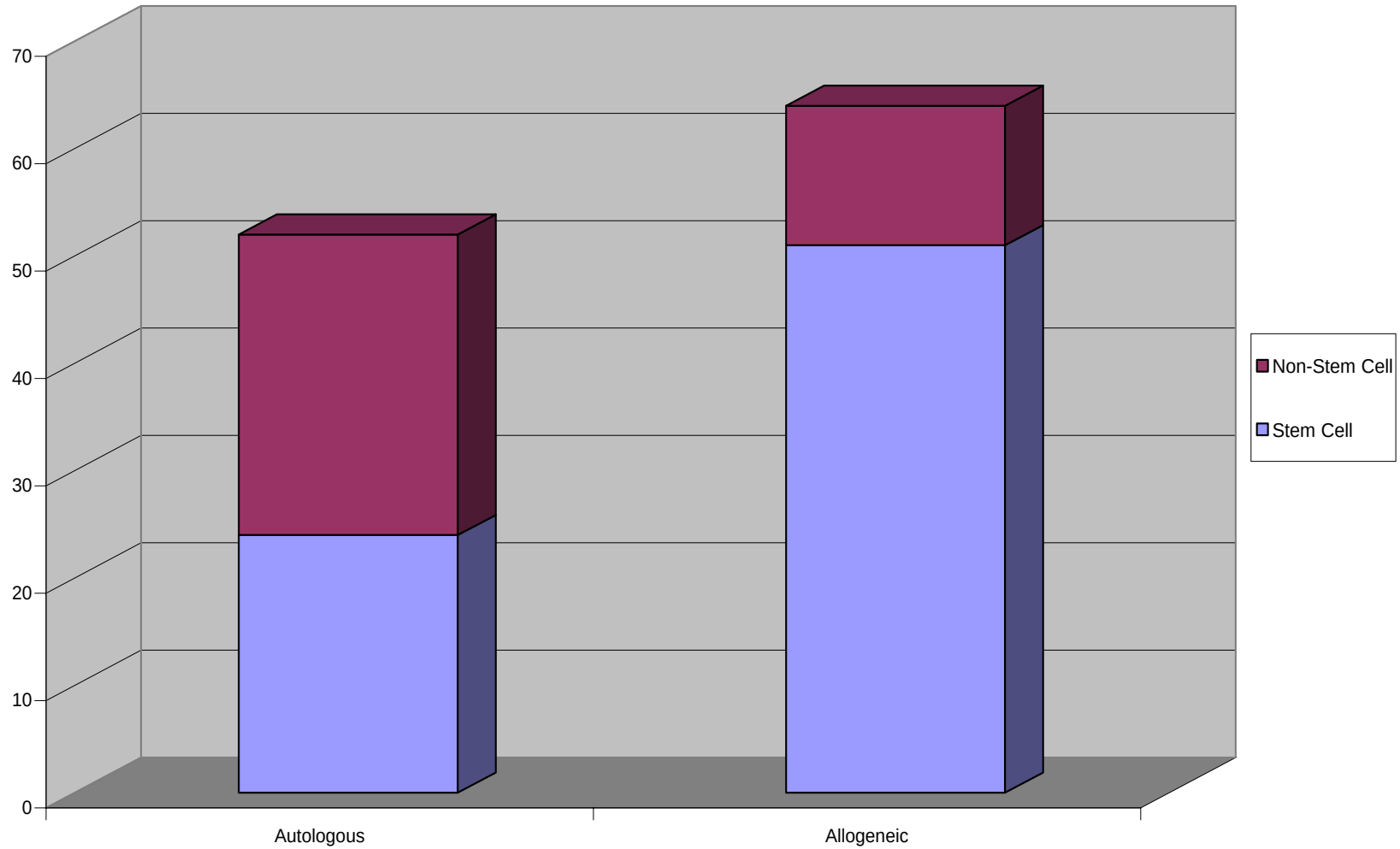
Primary cell therapy firms by disease indication



Primary stem cell firms by cell type



Primary cell therapy firms by autologous/ allogeneic distinction



Cell therapy products

- Primary firms with products on market are small – limited resources
- 5-10 years for product development
- Total sales (2007)
  - First generation (auto and allo) <$100M
  - Second generation (stem cells) <$ 25M
  - Secondary $750M
  - Cord blood banking $200M

SCIENCE · TECHNOLOGY · SOCIETY

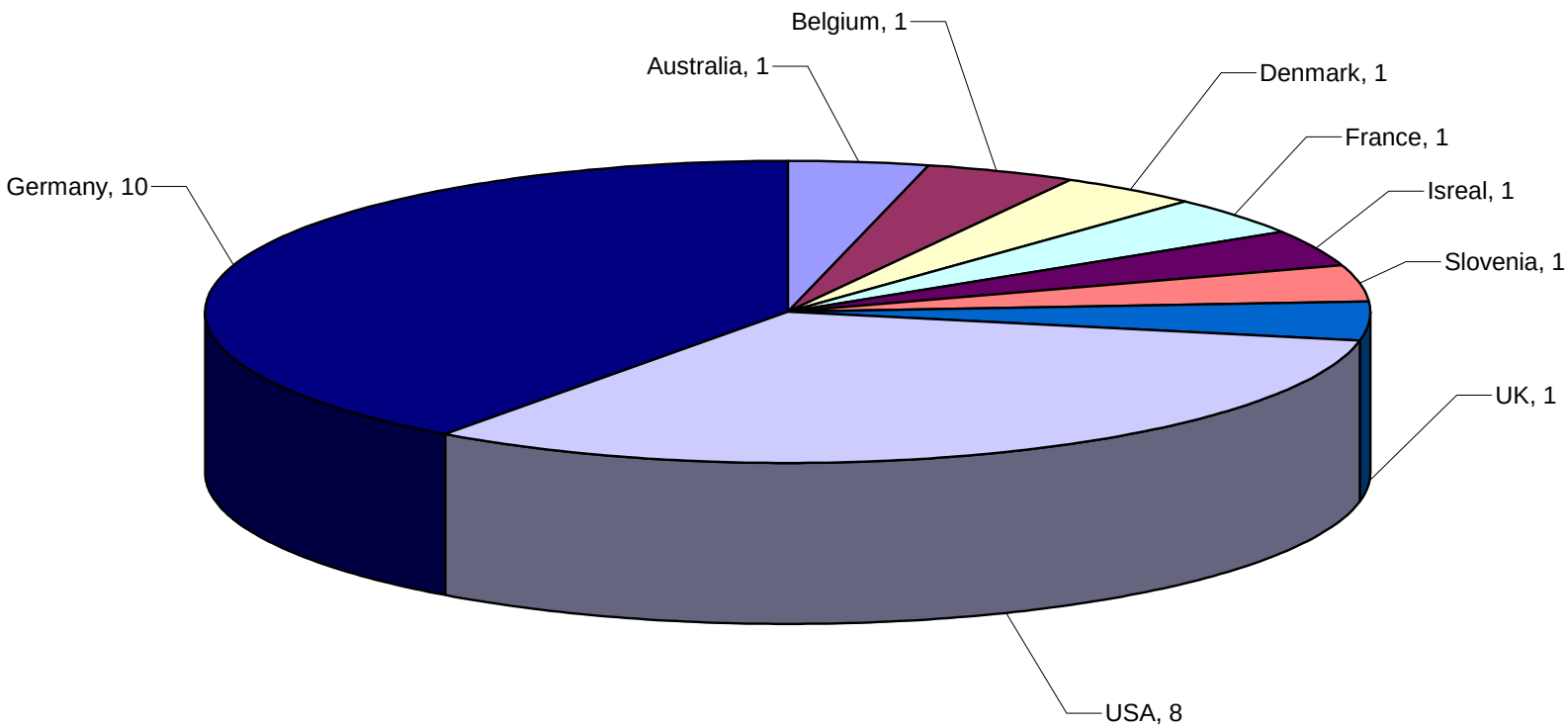
Products on market by type and application area

Application area	Primary – cell based		Secondary	TOTAL
	1st generation (non-stem cell)	2nd Generation (stem cell)	Matrices, scaffolds, gels	
Cartilage	13 (all auto)		2	15
Skin	7 (3 auto; 4 allo)	1	20	28
Bone	1 (auto)	1	32	34
Bone (dental)			11	11
Ophthalmic	1 (allo)		3	4
Aesthetic			1	1
Other			4	4
TOTAL	22	2	73	97

Sales of skin & cartilage products

Product	Company	Sales (2007)
Skin		
•Apligraf	Organogenesis	35,000 patients = ~$60M a year
•Dermagraft	Advanced BioHealing (Smith & Nephew)	$15M in 2003
•Epicel	Genzyme	700 since 1987
Cartilage		
•Carticel	Genzyme	<$28M p.a
•Chondrotransplant	Co.don	1,350 since 1996
•CaReS	Arthro Kinetics	1,000 since 2002

Primary products on market by firm location



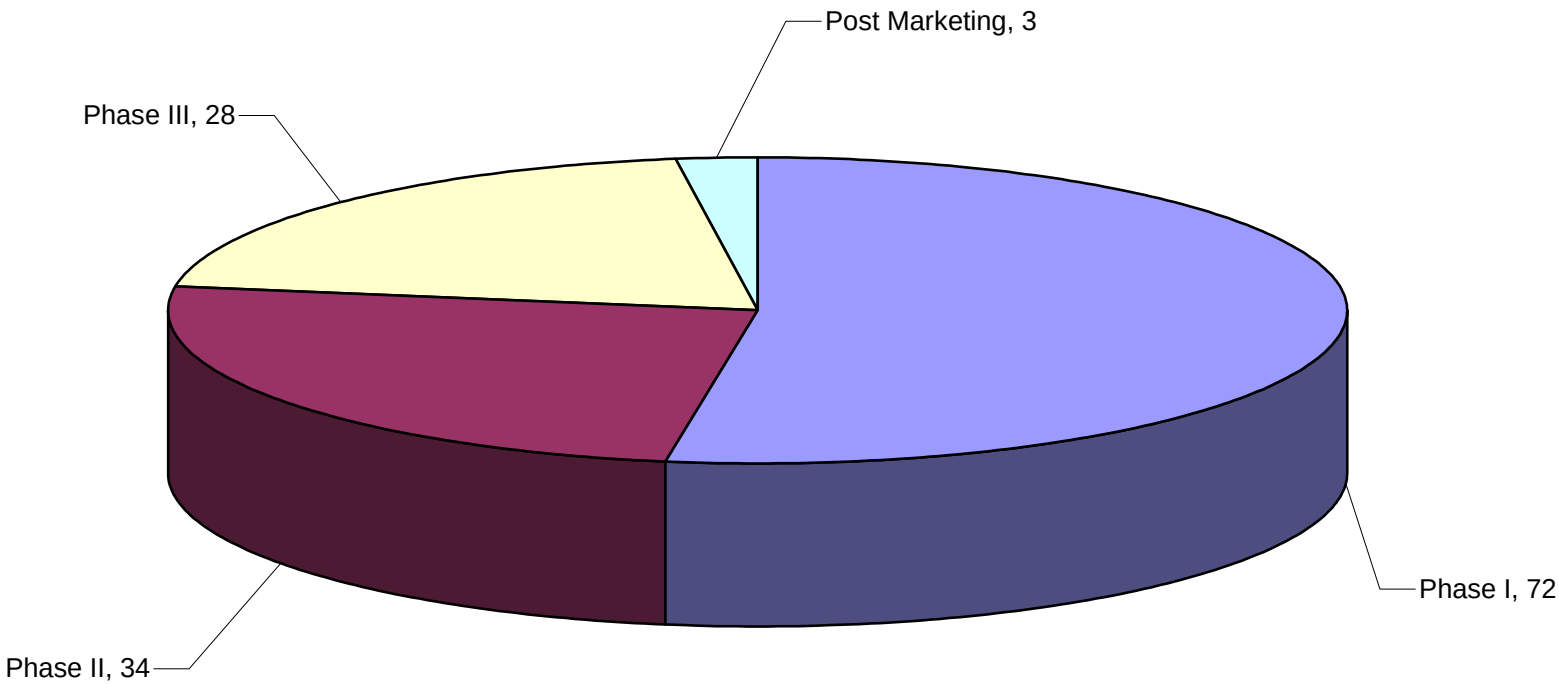
Industry pipeline

- 120 products in clinical development

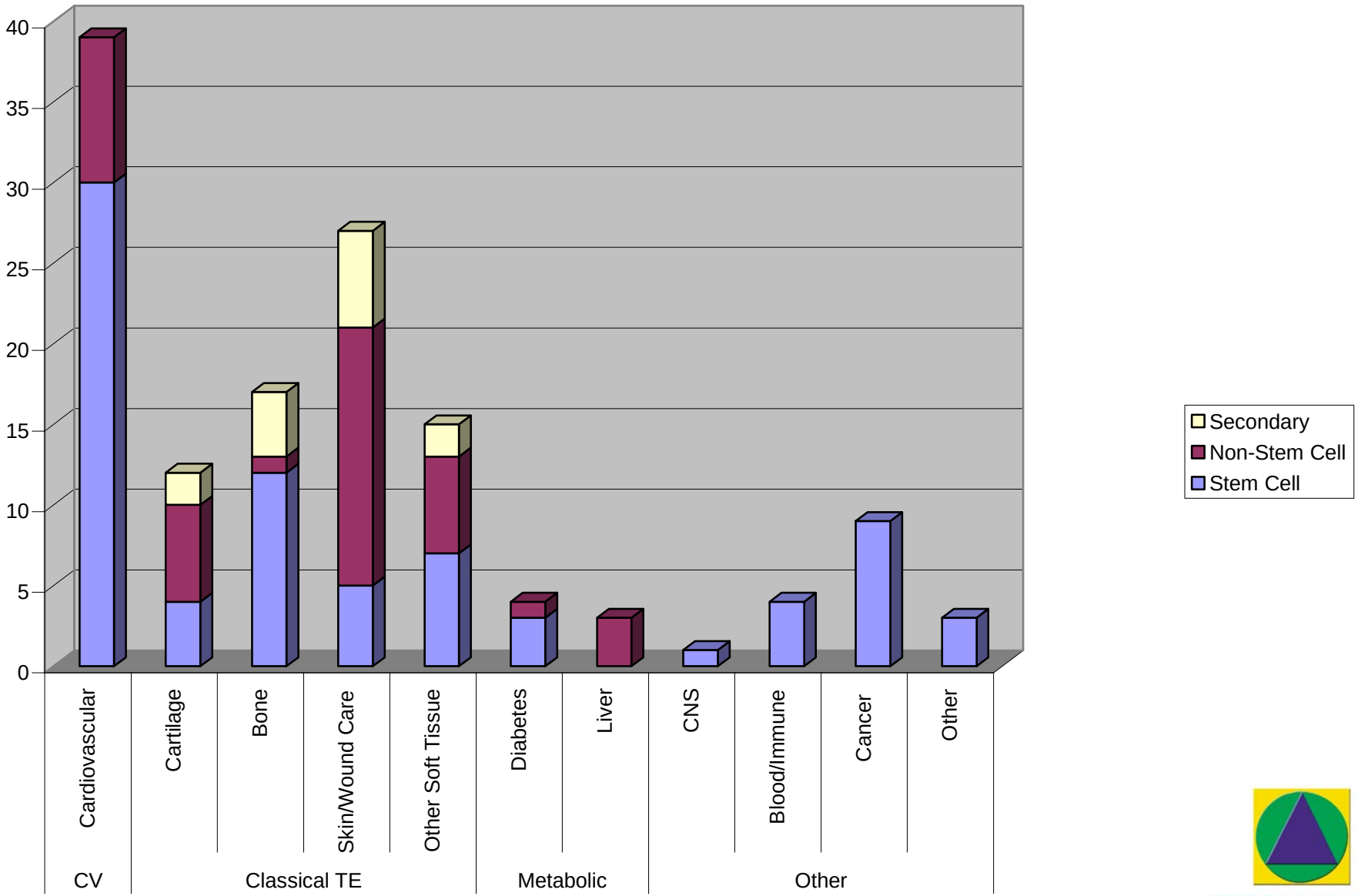
- Estimate based on industry standard figures:
  - 28 new products to reach market in 5-10 years
  - 16 for classical tissue engineering indications, six for CV diseases and six for others (mainly cancer)

SCIENCE · TECHNOLOGY · SOCIETY

Products by stage of clinical development



Products in clinical trial by disease



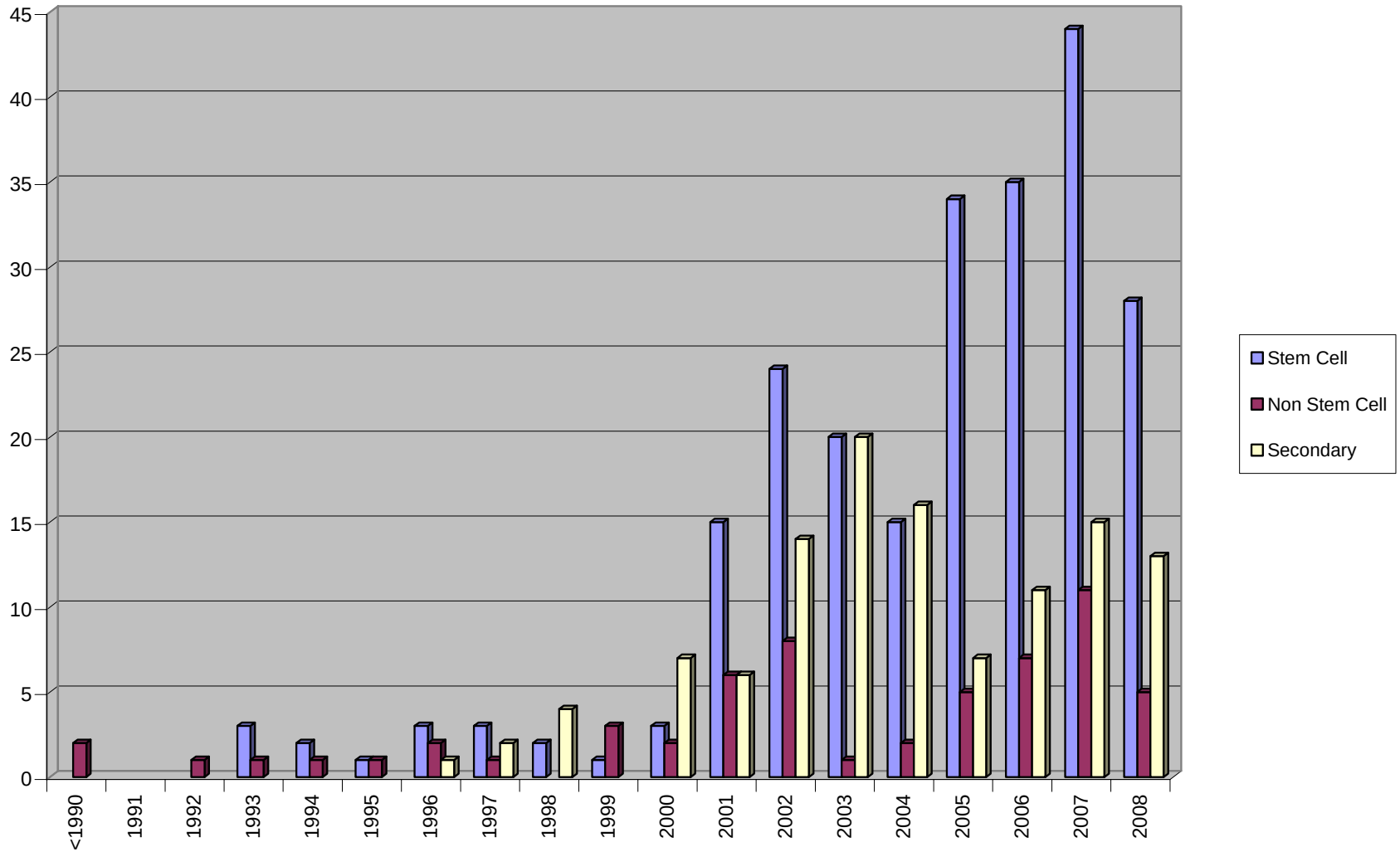
SCIENCE · TECHNOLOGY · SOCIETY

Pattern of industry collaborations

- 1987-2008 – total of 411 alliances ~ 20 a year (14% first generation firms; 57% stem cell firms; 29% secondary companies)
- Very few large deals >$10M
- Small number (99) of alliances with large companies (33% with biopharma; 50% device companies; 17% reagent & equipment companies)
- Only 9 biopharma companies involved in more than one deal – but signs of increasing interest

SCIENCE · TECHNOLOGY · SOCIETY

Cell therapy company alliances



Summary

- The number of firms has increased over the last five years, but high level of failure/ turnover
- Geographically concentrated - US, Ger, UK
- Relatively mature, but problem with firm growth
- Shift to SC as core technology (from TE to RM)
- Large number of products. Poor primary sales, but too early re SCs. Growing market for secondary
- Large number of products in development – mainly CV and classical TE
- Few collaborations with large firms
- Risk of market failure for some technical options

SCIENCE · TECHNOLOGY · SOCIETY

Why weren't products adopted?

- Multiple reasons
  - Lack of evidence base – cost-effectiveness
  - No better than established alternatives
  - Poor product specification (e.g. skin thickness, storage) & choice of disease/ clinical target
  - Difficulties fitting products into established routines
  - Reimbursement problems
  - High cost of manufacturing & distribution
- Central problem of clinical utility not being taken into account in product specification and design
- Main issues are structural/ institutional

SCIENCE · TECHNOLOGY · SOCIETY

Lack of user produce links

- History of first generation products - lack of interaction between developers and users
- Small science-based firms adopted rather linear model of innovation – poor understanding of user needs
- Success of Apligraf only after changed specification based on user feedback

SCIENCE · TECHNOLOGY · SOCIETY

Utility in practice

- Acceptance only possible if new technology demonstrates clear benefit over current practice
- Utility is framed by context (tacit knowledge) – severity of disease, cost-effectiveness, alternative treatments
- Utility constructed within existing work practices, routines, infrastructures and constrained by resources

SCIENCE · TECHNOLOGY · SOCIETY

The nature of clinical practice

- Medical work is deeply embedded in entrenched socio-technical regimes shaped by:
  - Management of complexity and uncertainty (about body and disease)
  - Established routines and interventions
  - Existing technical infrastructures (therapies, diagnostics)
  - Organisation of services and care
  - Rationed access to resources
- Medical knowledge is much more than the appliance of science
  - Other forms of knowledge are key and are only produced in particular clinical settings e.g. experience of disease, routines and protocols, practice style, complementary technologies, assessment of cost-benefit

SCIENCE · TECHNOLOGY · SOCIETY

The dynamics of translation

- Successful clinical development involves establishing clinical utility – multiple formal & informal criteria
- Importance of negotiating product specification and design with users to embed different forms of knowledge into artefact
- This is not as important in well established socio-technical domains & niches. e.g. ‘me-too’ drugs
- Unlike other technologies, users are constrained in ability to adapt technologies as they are used
  - Regulation, problem of re-engineering

SCIENCE · TECHNOLOGY · SOCIETY

Lessons for the future

- Successful innovation will require:
  - Overcoming major technical problems … but not sufficient to address structural issues
  - Viable business model – autologous (adult) cell therapy commercially unattractive?
  - Good product specification & design (user input)
  - Careful choice of clinical target (user input)
  - Regulatory certainty and innovation friendly procurement
  - Evidence base (cost-effectiveness)
  - Integration into existing practices & institutions
  - Scale manufacturing
  - Investment and collaboration with pharma/ device companies

SCIENCE · TECHNOLOGY · SOCIETY

Addressing market failure

- Reimagining the innovation process in therapeutics
  - Key role of public research in early stage clinical development – major source of innovation even in pharmaceuticals
  - Translational research as complex flow of different forms of knowledge between bench, bedside and firm

- New division of labour between public/ private sector
  - Change in policy focus – underwriting risk, cost & benefit sharing, greater steering to maximise public health gains?
  - Creating public sector innovation infrastructure

SCIENCE · TECHNOLOGY · SOCIETY

Final thoughts

- Need a better understanding of the dynamics of translation – insights from sociology of knowledge
- Rethink the innovation process in emerging biotechnologies
  - Key role of public sector in addressing market failure
  - Slow pace of change in clinical practice – institutional barriers
- Role of social scientists?
  - Telling inconvenient truths
  - Engaging with innovators, but maintaining critical distance
  - Ensuring realistic expectations – role of scepticism in a promissory field? Need for reflexivity.

SCIENCE · TECHNOLOGY · SOCIETY