HOW CALIFORNIA TOOK THE LEAD IN THE GLOBAL GROWTH OF STEM CELLS AND REGENERATIVE MEDICINE

Annika Rickne

Professor of Innovation, Entrepreneurship & Industrial Dynamics

Affiliated to

Royal Institute of Technology

Chalmers University of Technology

NOVELTY CREATION IS RISKY BUT POTENTIALLY BENEFICIAL

- Highly novel inventions - radical, disruptive, discontinuous, paradigmatic, breakthrough
- Can provide great benefits to firms and inventors as the innovations create new markets and economic growth (Schumpeter, 1942; Christensen, 2010)
- But novel inventions are
  - less likely to be commercialized
  - more likely to fail in the market
  - more likely to kill the first mover firm
  - more likely to give benefits to dominant incumbents
  - Astebro & Dahlin, 2005; Tellis & Golder, 1998, Teece, 1997
- Success factors: e.g. resources, control of complementary assets, and a strong network position are important

IT IS SO VERY DIFFICULT FOR A FIRM TO SUCCEED IN RADICAL INNOVATION!

BUT IF WE DO IT TOGETHER?

REGIONAL CLUSTERS

WITH ACTORS DOING

NOVEL INVENTIONS & RADICAL INNOVATION

AREAS OF RADICAL INNOVATION IN A REGION: BUILDING **CLUSTERS**

Which factors can help regions to be successful in terms of building resilient clusters with actors doing highly novel inventions & radical innovation?

- **Universities** as **motors**
- **Large firms** as **motors**
- **Social networks** and **knowledge flows**

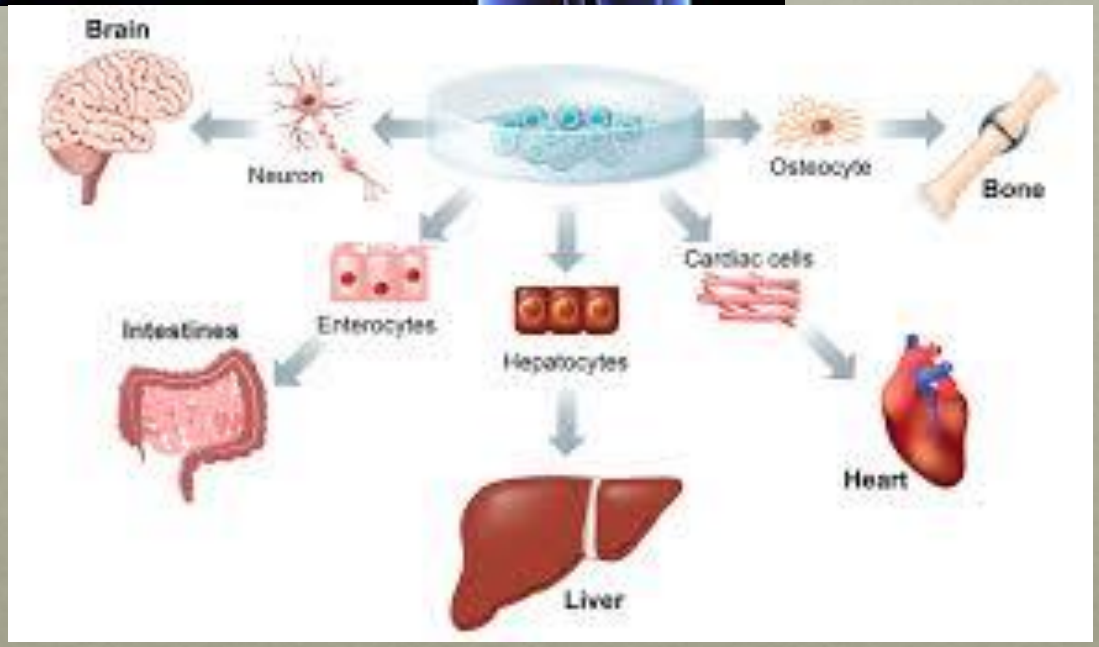
My argument: We need to go **beyond traditional explanations**

THE CASE OF

STEM CELLS AND REGENERATIVE MEDICINE

- **Stem cells and regenerative medicine globally**
  - Builds on longitudinal data from 1997 and on
  - California, Massachusetts, Ohio, Sweden, Germany, UK, Japan
  - Qualitative approach
  - Around 200 interviews globally
  - Secondary data on publications, funding, firm strategies, policies
- The case of **California Institute of Regenerative Medicine**, from 2004

=> **New avenues for understanding of clusters**


Brain
Neuron
Osteocyte
Bone
Cardiac cells
Enterocytes
Intestines
Hepatocytes
Heart
Liver

RADICAL INNOVATION

LARGE POTENTIAL BUT MANY HURDLES

Scientific uncertainty

Long time scales

Technological development tools

Manufacturing & scale up

Heavy regulatory burden

Uncertainty of reimbursement

Business models: type of cell source, role in a value chain, location

Lack of legitimation

Market, buyer

Investments lacking

- Too early for large firms
- Too expensive & complex for new firms
- Government investments increasing but still insufficient

Critical mass, Clustering

CAN ONE CREATE A CLUSTER?

High potential: Cures, improved health, growth

- USA and CA not starting from zero in the field
- But due to Bush's ban 2001 there was a risk of loosing this advantage (scientists leaving, investments decreasing, etc.)

Can one create a cluster?

CAN ONE CREATE A CLUSTER?

Can one create a cluster?

Yes: Regional policy practices ? + Normative research?

No, not without solid starting conditions: Porter & the innovation, economy and geography literature at large

The questions are rather:

What is required for a region to build a resilient cluster based on its initial resource base ?

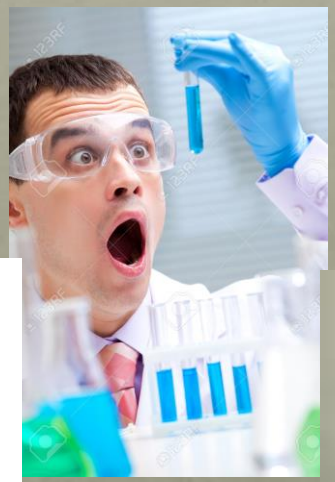
Is coordination, governance, orchestration valuable, or should the process be spontaneous and bottom-up?

A NEW ORGANIZATIONAL INNOVATION
CALIFORNIA INSTITUTE OF REGENERATIVE MEDICINE, CIRM

- 2004: Proposition 71, 10-15 year program => Cures & jobs
- Large-scale R&D funding model at the state level with publicly supported bond issues, $3 billion USD

Infrastructure, Education

Scientific discovery, Translational research, Clinical trials



SITUATION IN CA TODAY: RESEARCH

- Very good scientific progress, Addressing bottlenecks
- Data sharing & Large studies
- Discussion in wide and multi-disciplinary academic community
- Co-funding attracted
- Move towards clinic
- Stem cells legitimized as part of overall cell science

Established Goals	Delivered Results	
 NEW THERAPEUTICS CANDIDATES DISCOVERED	 16	We obviously didn't set the bar high enough, because we achieved this goal, then exceeded it by more than 50 percent. Next year, we step up our game even more.
 PROGRESSION EVENTS	 16	We want to fund the most promising science and make sure it successfully progresses to the next stage of development—a Progression Event. This year we did just that.
 ESTABLISH NEW REGULATORY PARADIGM	 YES	Getting the FDA, Congress, and the President all to agree on a new approach to stem cell regulation (the 21st Century Cures Act) was not an easy task. But in the end the combined efforts of many different groups—including CIRM—did just that, and on December 13, 2016, it was signed into law.
 CREATE STEM CELL TRANSLATING & ACCELERATING CENTERS	 YES	This year CIRM combined and opened both centers in a unique way to help the most promising research progress out of the lab and into clinical trials faster.
 NEW CLINICAL TRIALS	 10	At midsummer we had only two clinical trials approved, and lowering our standards was not an option. Team Therapeutics (one of the groups charged with this goal) looked to be in trouble. But they staged a dramatic fourth-quarter comeback and achieved their goal in December.
 PARTNERED CLINICAL PROJECTS	 2	With two partnerships, we made significant progress but fell short on this goal. We're working to complete the job and secure the third partnership in 2017.

SITUATION IN CA TODAY

INFRASTRUCTURE OF RESEARCH

- Physical infrastructure
- Human infrastructure
- Some places have built capabilities from scratch
- Training on a larger scale, train people who can become PI's
- Inter-disciplinarity
- Researchers from peripheral or new fields can come into the field – and subsequently find financing from other complementary sources
- Moves from a narrow focus on stem cells – but builds an infrastructure on larger/broader issues – the cell, genomics, etc.

SITUATION IN CA TODAY

CLUSTERING OF RESEARCH

- Geographical agglomerations of critical mass at universities – at three places. (But are they connected to one another?)
- Some interconnections between universities & institutes
- Collaboration between high & lower ranked universities
- Research in small & large firms
- Firm – Institute – University – Hospital collaboration
- Spurred additional investments by other actors
- Philanthropy links money with patient advocates, researchers, firms

SITUATION IN CA TODAY
FROM BENCH TO BEDSIDE

- Basic research - Translational research – Clinical research
  - Finding & realizing applications
  - Separation due to disciplines, publication patterns =>

    Multi-disciplinary collaboration needed
  - Multi-skill teams already in research phase: basic science, clinic, patient needs, firm strategy, financing, regulation, manufacturing, scale up
  - Findings from several studies, data sharing

SITUATION IN CA TODAY
FROM BENCH TO BEDSIDE

- Educational process for scientists: Transitional research, On patient needs, On industrial needs & realities
- Priorities changed on university/institute level: Translational work in focus, Incentives
- Change in firms: New types of collaborative teams
- Regulatory pathways discussed and lobbied

SITUATION IN CA TODAY

ATTITUDE CHANGES

- Attitude changes
  - An outcome of CIRM is that the public has become educated: high school students, etc.
  - Scientists as citizens – engaging in debates and political goals
  - There is large public support for science
  - The patient advocates seems very patient
  - Resistance today? Not sufficient results?

THE LITERATURE HOLDS TRUE
UNIVERSITIES & FIRMS & NETWORKS AS MOTORS

The literature on innovation management, innovation policy, economic geography, entrepreneurial universities, innovation systems the triple helix approach:

- **Universities** gives regional knowledge spill-overs
  - Leading academic and clinical scientists, entrepreneurial universities, strong industrial networks, experience from commercialization, strong management, directed initiatives
- **Large firms** can act as motors in a regional economy
  - Strong industries, large firms, complementary assets, pooled labor market
- **Networks and knowledge spillovers**
  - Open innovation approaches
  - Intense interaction between universities and hospitals, univ & firms, large and small firms

True but not
sufficient.

Perhaps too focused
on structure?

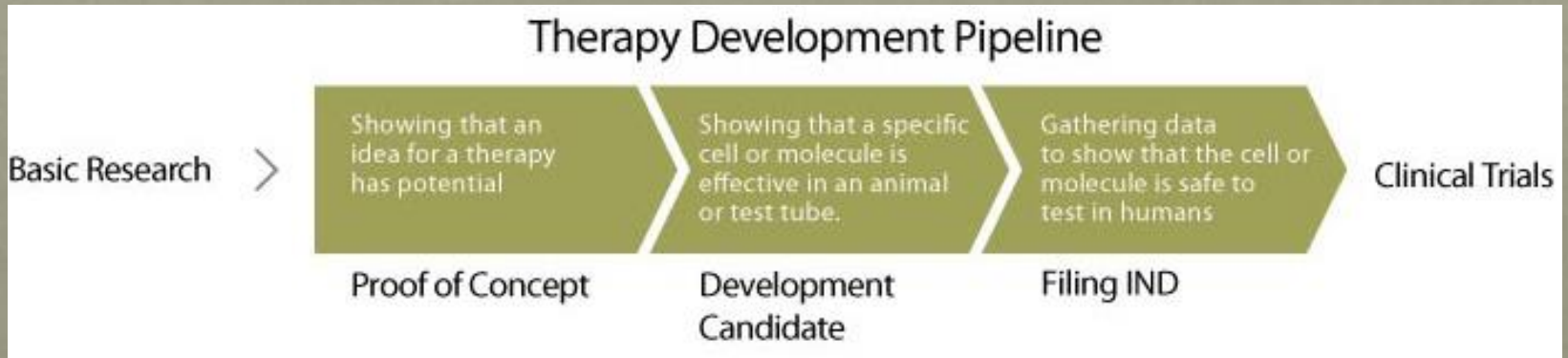
Towards a more
dynamic approach
to cluster building

A. Recognizing the character of knowledge production

- **A full set of complementary actors**: Researchers – universities, institutes, Hospitals, Patients, patient advocates, Financing bodies (NIH, NSF, CIRM), Business angels, VC, philanthropy, Large & small firms
- **Additional people** recruited globally & **new firms** started
- **Changing roles** of the ecosystem: Recognition of **trajectories:**
  - Motivations, how ideas develops, how research connects to policy processes, pursued through academia, firms or some combination, the move to translational research.
  - Firms take on tasks that academia usually do (e.g. research developed in industry, transferred to academia for 'free')
  - Academia take on tasks that firms usually do (trials, business plans)
  - Users influence development paths

A. Recognizing the character of knowledge production

- Addressing the complete development process
- Getting products to the bedside
- The interaction of large and small firms, universities and hospitals. Open innovation and an hybrid firm-academic entity
- Expanding and diversifying from technology specific cycles: Broader knowledge and product base



B. EXPERIMENTING VS. SELECTING A WINNER

- Evolutionary development: Variety creation & experimentation
- Selection & retention processes: Should anyone select a winner?
- Policy involvement – but driven by scientists, firms, peers, citizens, consumers, patients
- Experimenting to find winners: Has its own underlying goal – push in a certain direction
- Decision making models & strategic choices the operation of CIRM: A customer and patient driven approach
- Experimentation: Scaling up of research & trials
- Business orientation: Milestone driven vs. hypothesis driven

C. Counter-cyclical financing model

- Funding for the earliest stages of discovery, "Valley of Death", before private industry gets involved
- Verify therapies and begin clinical trials
- Counter-cyclical financing model transcends negative effects of business cycle downturn on yearly legislative decision-making for R&D spend
- A direct democracy provision
- Accountable to citizens and to the board
- Gives persistence

D. VISIBLE AND PROACTIVE REGIONAL LEADERSHIP FROM ALL SPHERES

Not top down cluster formation, but support for resilience

CIRM as a coordinator: Framework for actors to influence & interact.

Supports PI to avoid hurdles, Strategic advice, Networks, Complementary assets, Financing

E. INVOLVEMENT OF CITIZENS

Scientists engage with elites and broader coalitions, enhancing their role in society

Researchers as lobbyists & citizens

Innovation processes

Citizens become more knowledgeable about science & engage with scientists as relative equals

Patient advocates & users. Stability of purpose. Active in scientific and financial choices

Citizens as initiators and end users
Market pull

Towards a more dynamic approach to cluster building

What is required for a region to build a resilient cluster based on its initial resource base ?

- Universities & large firms as motors
- Social networks & knowledge flows
- Recognizing the character of knowledge production & Changing roles
- Experimenting to find winners
- Persistent financing model
- A visible and proactive regional leadership from all spheres
- Involvement of citizens

Is coordination, governance, orchestration valuable, or should the process be spontaneous and bottom-up?

- Both. Government can not orchestrate. All stakeholders needed