Academic Perspective on Clinical Development of Novel Cell Therapies

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Early Clinical Development of Novel Cell Therapies

- Value of academic centers
  - Motivated, scientifically-oriented clinical investigators
  - Basic science infrastructure – great for ancillary studies to evaluate disease mechanisms, discover new assays & biomarkers, etc
  - Clinical research infrastructure (IRB, DSMB, biostatistical support, clinical coordinators, etc) often excellent for early phase trials
Early Clinical Development of Novel Cell Therapies

Where are the resources for product development & early phase trials?

- In past, cell therapy development was done by “borrowing” resources (staff, space & equipment) from BMT clinical & research labs
- Some development funded by companies, but
  - Academic vs commercial agendas differ
  - IP is an issue
- NIH grant funding – limited, but NHLBI established PACT to fill gaps
- CIRM grant funding – for stem cell initiatives
Example: MSCs for Acute Lung Injury (ALI)

- ALI is a common clinical condition with high morbidity and mortality

- Preclinical discovery research by clinical investigator, M Matthay MD (UCSF)
  - BM-derived MSCs obtained from Prockop lab (research grade)
  - Models
    - Rodents with lung injury
    - Ex vivo perfused human lung injury model
    - In vitro model of injury to type II alveolar cells
  - Data suggests beneficial effect of bone marrow derived MSCs in ALI in these models (mechanism probably paracrine)
MSCs for ALI – Existing funding

- Matthay – principal investigator
  - RO1 grant from NHBLI/Lung Division
  - Multi-center consortium for phase II clinical trials in ALI from NHLBI/Lung Division

- Other funding at UCSF
  - NIH/NCRR Clinical & Translational Science Award (CTSA) – infrastructure grant
    - BREAD Program (biostatistics & research design)
    - RKS (regulatory support)
MSCs for ALI – New funding

- CIRM – applied Feb 2008
  - Disease Team Planning Grant
  - Review positive, not funded

- PACT/NHLBI – applied Sept 2008
  - Clinical-grade MSCs for IND-enabling studies & manufacturing for clinical trial
  - Reviewed & approved by Nov 2008
  - U of Minnesota started manufacturing Jan 2009
  - Cells shipped to UCSF April 2009

- NIH/NLBI Challenge Grant – applied May 2009
  - For pre-IND studies, more science & mechanistic studies, and clinical trial
  - Collaboration UCSF & U of Pittsburgh
Issues for Academic – Industry Collaborations in Cell Therapy Development

- Development and manufacturing by academic facility vs company
  - Do you want to commercialize?
    - Consider requirements for preclinical stage vs early phase trials vs late phase trials and BLA
  - Does a proprietary product formulation inhibit scientific progress?
  - Do you want to compare different formulations?

- Reformulation or reworking of product by academic collaborator
  - Intentional - genetic manipulation, delivery devices/combination products
  - Unintentional?
Issues for Academic – Industry Collaborations in Cell Therapy Development

- Assay development
  - academia often positioned for interesting science
  - companies usually better than academia at validation

- GLP for preclinical animal studies
  - CRO vs academic labs?

- Product handling at clinical site
  - Understanding of quality systems, CGTP
  - Receipt & storage
  - Thaw, wash, transfer to delivery device
  - In-process testing
  - Reality check on stability studies