Drug Discovery at UC Campuses

Is there a Common Vision?
# Impact of public sector research on pharmaceutical industry

<table>
<thead>
<tr>
<th>Discovering Institution</th>
<th>Number</th>
<th>Current Marketer</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institutes of Health</td>
<td>22</td>
<td>GlaxoSmithKline</td>
<td>12</td>
</tr>
<tr>
<td>U. of California</td>
<td>11</td>
<td>J&amp;J</td>
<td>9</td>
</tr>
<tr>
<td>Sloan Kettering</td>
<td>8</td>
<td>Bristol-Myers Squibb</td>
<td>8</td>
</tr>
<tr>
<td>Emory University</td>
<td>7</td>
<td>Merck</td>
<td>8</td>
</tr>
<tr>
<td>Yale University</td>
<td>6</td>
<td>Pfizer</td>
<td>8</td>
</tr>
<tr>
<td>Children's Hospital, Boston</td>
<td>5</td>
<td>Eli Lilly</td>
<td>6</td>
</tr>
<tr>
<td>MIT</td>
<td>5</td>
<td>Genzyme</td>
<td>6</td>
</tr>
<tr>
<td>Salk Institute</td>
<td>5</td>
<td>Novartis</td>
<td>6</td>
</tr>
<tr>
<td>Wisconsin Alumni Research Foundation</td>
<td>5</td>
<td>AstraZeneca</td>
<td>5</td>
</tr>
<tr>
<td>Columbia University</td>
<td>4</td>
<td>Wyeth</td>
<td>5</td>
</tr>
<tr>
<td>New York University</td>
<td>4</td>
<td>Amgen</td>
<td>4</td>
</tr>
<tr>
<td>U. of Michigan</td>
<td>4</td>
<td>Bayer Healthcare</td>
<td>4</td>
</tr>
<tr>
<td>U. of Minnesota</td>
<td>4</td>
<td>Eisai</td>
<td>4</td>
</tr>
<tr>
<td>U. of Texas</td>
<td>4</td>
<td>Roche</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abbott</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baxter Healthcare</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BiogenIdec</td>
<td>3</td>
</tr>
</tbody>
</table>

From The Contribution of Public Sector Research to the Discovery of New Drugs, A. Stevens et al, Boston University, 2009
Impact of public sector research on pharmaceutical industry

- 2008 US Sales $36.9 billion
  - 21 products no longer sold
  - >$1 billion 13
  - >$2 billion 4
  - >$3 billion 2

Source: IMS Health

From The Contribution of Public Sector Research to the Discovery of New Drugs, A.Stevens et al, Boston University, 2009
Innovation Ecosystem: Drug Discovery and Development

- Knowledge Creation and Dissemination
- Faculty development
- Facilities and Infrastructure
- Students, workforce development

- IP
- Translational activities
- Startups
- Licensing

- Pipeline diversification

- Commercial Development
- Preclinical package
- Clinical Trials
- Product Launch
- Workforce Development

Adapted from A. Pradhan “Technology Transfer: building and maintaining relations with Industry”
Opportunities for UC collaboration

- On all levels of Innovation Ecosystem, such as:
  - Sharing education and workforce development
  - Complementary facilities and infrastructure
  - Collaborative translational activities
  - Master Research/CT agreements
  - Linking EMR
  - Multicenter Clinical Trials
  - Disease Consortiums
Drug Development Process

Target ID and Validation

HTS, Lead Generation and Optimization

Candidate preclinical development

Phase I-IV

NDA review and FDA approval

Post-Marketing line expansion

Biological Hypothesis
In vitro and in vivo studies

Assay development
Library synthesis
Target screening
Medicinal chemistry
In vitro tox

Animal Tox, PK and PD
Chemistry, Manufacturing and Controls

Protocol development
IND submission
Example of Academic Drug Development

- Allopregnanolone for treatment of TBI
- 174 patients, single center trial
- $7.7M DOD Award
- $1.73 /2 years
- Pre-IND and IND submitted
  - 350 pages
- **Subcontractors & Consultants**
  - Scientific/Clinical
  - Regulatory
  - Manufacturing
  - Formulation
  - Biostat
  - Clinical Monitoring
- **Pre-clinical tox or efficacy was not required** (published lit)
Example of UC Collaboration: complementary facilities and resources

Target ID and Validation
HTS, Lead Generation and Optimization
Candidate preclinical development
Phase I-IV
NDA review and FDA approval
Post-Marketing line expansion

Multiple Genomics, Proteomics and Metabolomics screening facilities
Animal Models of Disease
Tissue Banks

Some Cool Stuff:
• Primate Center (UC Davis)
• Crump Institute for Molecular Imaging (UCLA)
• Beckman Laser Center (UCI)
• Stem Cells (UC Davis, UCSF)
• DXMS Proteomic Resource (UCSD)
Example of UC Collaboration: complementary facilities and resources

- Target ID and Validation
- HTS, Lead Generation and Optimization
- Candidate preclinical development
- Phase I-IV
- NDA review and FDA approval
- Post-Marketing line expansion

Some Cool Stuff:
- SiRNA of druggable genomes at Molecular Screening Shared Resource (UCLA)
- Small Molecules Discovery Center (UCSF), incl. Med Chem capabilities
- OBOC screening (UC Davis)
- Cal Nansystems Institute (Drug delivery –UCLA)
- Natural Product Libraries (UCSD)
- Computer-aided DD group (UCSD)
- Structural and Medicinal Chem database (UCSD)
Example of UC Collaboration: complementary facilities and resources

- Target ID and Validation
- HTS, Lead Generation and Optimization
- Candidate preclinical development
- Phase I-IV
- NDA review and FDA approval
- Post-Marketing line expansion

Some Cool Stuff:

- cGMP facility (UC Davis) – production of phase I-II quantities of small molecules, cellular therapies and biologics
- GLP Tox infrastructure at Animal Care Program (UCSD)

Animal ADME/TOX
In vitro tox screens
Large-scale chemical and biological synthesis
Summary: complementary facilities and resources

Target ID and Validation
HTS, Lead Generation and Optimization
Candidate preclinical development
Phase I-IV
NDA review and FDA approval
Post-Marketing line expansion

**Strong position**
- Many individual capabilities, including genome/proteome facilities, optical cores, animal models
- Several Chemistry cores, multiple chem libraries, at least one MedChem core

**Reasonably strong position**

**Limited Position**
- Limited GLP tox capabilities
- One cGMP facility; limited formulation capabilities
UC Opportunities for Collaboration in Drug Discovery and Development

- **Strong position in target id and validation**
  - Typical academic strength
  - Catalogue and make known the available resources (especially Animal Models) (Susan Old)
  - Disease-specific teams
UC Opportunities for Collaboration in Drug Discovery and Development

- **Reasonable position in small molecule screening and assay development**
  - Streamlining the mechanisms for collaboration
  - Catalogue and make known the available resources (what compounds are available, especially unique)
  - Sharing and integrating libraries and capabilities
  - One point person from each screening center
  - IP issues in Med Chem
  - Commercial vendors (outsourcing); preferred pricing
  - Academic Med Chem coaches and project managers
  - One coordinating center for UCs
UC Opportunities for Collaboration in Drug Discovery and Development

- **Limited position in Preclinical Development**
  - Two cGMP facility (UC Davis, UCLA) is enough to supply the system
  - One GLP tox program (UCSD) potentially enough, infrastructure need to be expanded
  - Explore outsourcing capabilities for ADME and Tox
  - Commercial vendors vs academic coaches
  - One UC coordinating center
  - Limited funding available for these studies
Action Items

- Explore NIH list of animal models (Susan Old)
- Funding individuals from each UC to catalog animal models
- One point person from each screening center to catalog and define potential shared resources
- Review MedChem outsourcing (UCSF)
- Review ADME/TOX outsourcing (UCSF)