The Value of Tissue Banks to Drug and Dx Developers

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Conflicts of Interest, Privacy/Confidentiality, and Tissue Repositories: Protections, Policies, and Practical Strategies

Tissue Banks for Tx and Dx Developers: What is the need?

- Basic research: the biological revolution in the medicinal chemical industry
  - Drug targets
  - M
  - B
- Clin pharmacogenetic/genomic profiling
  - Toxicity
  - Drug responsiveness
  - Rescuing failed drugs

PGx will drive the collection and use of stored tissues into common practice involving millions of subjects

What is needed from tissues?

- DNA: gene, SNP, population association
- RNA: gene expression array or profiling
- Proteins: proteomics
- Cell morphology: pathology

Pharmacogenetics Is….

- The influence of genetic traits on the magnitude or type of *toxic effects* of drugs.
- The influence of genetic traits on the magnitude or type of *therapeutic effects* of drugs.
- A genetic determinant of overall drug response; not a measurement of physiological status!
- PGenetics: Targeted study of gene variants determining drug response
- PGenomics: Genome wide study of genetic determinants, including the study of gene expression (requiring RNA as a study material)

FDA Guidance on PGx

- PGx will "help individualize therapy with the intent of maximizing effectiveness and minimizing risk."
- Important "that FDA policy *facilitate, not impede*, the use of pharmacogenomic tests during drug development and, to the extent possible, encourage open and public sharing of data…on PGx test results."
- "most experimental results may not be well enough established to be suitable for regulatory decision making"

FDA Guidance on PGx

- "the FDA is *encouraging voluntary submission* of such data…"
- "As…field of PGx advances, it is likely (*and desirable*) that sponsors will begin to use PGx tests to support drug development and/or to guide therapy"

Developing tests for marketed drugs

- Currently available drugs could be targeted to appropriate patients
- Leads to:
  - Need for archival repositories with clinical records of all drug therapies
  - Need to revisit stored tissues from prior clinical trials (as in original drug trials)
  - Need to attach PGx testing to Phase III/IV studies

BIO perspectives, recommendations

- Review commensurate with risk; a two tiered review system
  - Research involving intervention or interaction
  - Research using medical records and tissue archives
- Federalize regulations/laws governing consent, use and retention of tissue to make consistent with all regulations (not State by State)

BIO perspectives, recommendations

- Subject's authorization or specification of limitations on permissible uses of data and biological materials must be respected.
  - E.g. Right to withdraw at any time must be honored

Sample PhRMA perspectives on privacy in tissue research

- Medical information, including genetic information, should have equal protection
- Researchers must have unrestricted access to anonymized or encrypted patient information
- Uniform national requirements should govern biomedical research, although individual states should be able to prescribe additional penalties for violations of privacy

Example Tissue Repositories

- Cooperative Groups (such as the Cooperative HumanTissue Network)
- Ardais
- GeneLogic
- International Genomics Consortium
- IMPATH
- Integrated Lab Services

Example Tissue Repositories

- LifeSpan Biosciences
- Oncotech
- PathServe
- The AlphaOne Foundation
- Genomics Collaborative
- Duke Center for Human Genetics
- Cancer centers

What is an appropriate posture or role for IRBs to take in this arena?

- IRBs represent the "interests" and welfare of subjects
  - Gifting for the development of better medicine
  - Do me no harm
  - Allow me to understand my risks
  - "Willing suspension of autonomy"?
- What is risk of NOT suspending autonomy?

How suspension of autonomy may lead to useful discoveries

- Complex test to profile newly diagnosed women with breast cancer re risk for recurrence. (Genomic Health, Inc.)
  - Genetic risk factor for MI (DeCODE)
- New drug into development for MI targeted at genetic risk factor for MI (DeCODE/Bayer)
- New test for responders to Iressa among non-small cell lung cancers

How suspension of autonomy may lead to useful discoveries

- Collecting DNA for unknown future use:
  - New test in development for response to treatment with statin drugs: personalized medicine (Gennaissance;Abbott Labs)