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Data-related Challenges of Genotype - Phenotype studies

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Introduction and Question

- Genome wide association studies
  - ✓ genotyping constantly gets cheaper
  - ✓ many formerly phenome-related projects around complex diseases consider genotyping within the next couple of years.
- challenges
  - A) sufficient case/control numbers
  - B) high quality patient material to be genotyped
  - C) high quality phenotype data
  - D) how can we homogenize the heterogeneous data sources?
  - E) privacy problems!

C) Phenotype data?

- many disease related data collections in the form of registries (phenotype) or biomaterial collections (poss. genotyping)
- Biomaterial banks is likewise scattered due to ethical and legal reasons
- genotyping prices constantly go down, (good) phenotypic annotation is expensive
- The phenotype data could either be captured via
  - ✓ clinical trials
  - ✓ phenotype data from hospital data bases - taking into account the quality uncertainty
  - ✓ phenotype data from disease-related registries.

D) Homogenization

- The challenge starts as soon as genotype and related phenotype data from different data sources are available for further analysis.
  - ✓ Genomic data tends to be more structured than phenotype data, Bioinformatics community is open source and XML based
  - ✓ Phenotype data is kept mostly in traditionally “hand carved”, non-compatible Information systems

- For association studies not only the **data formats** have to be homogenized, more importantly the **content** has to be homogenized. Ontology-approaches using UMLS had some success recently

Butte, A.J. and I.S. Kohane, *Creation and implications of a phenome-genome network.* Nat Biotechnol, 2006. 24(1): p. 55-62.

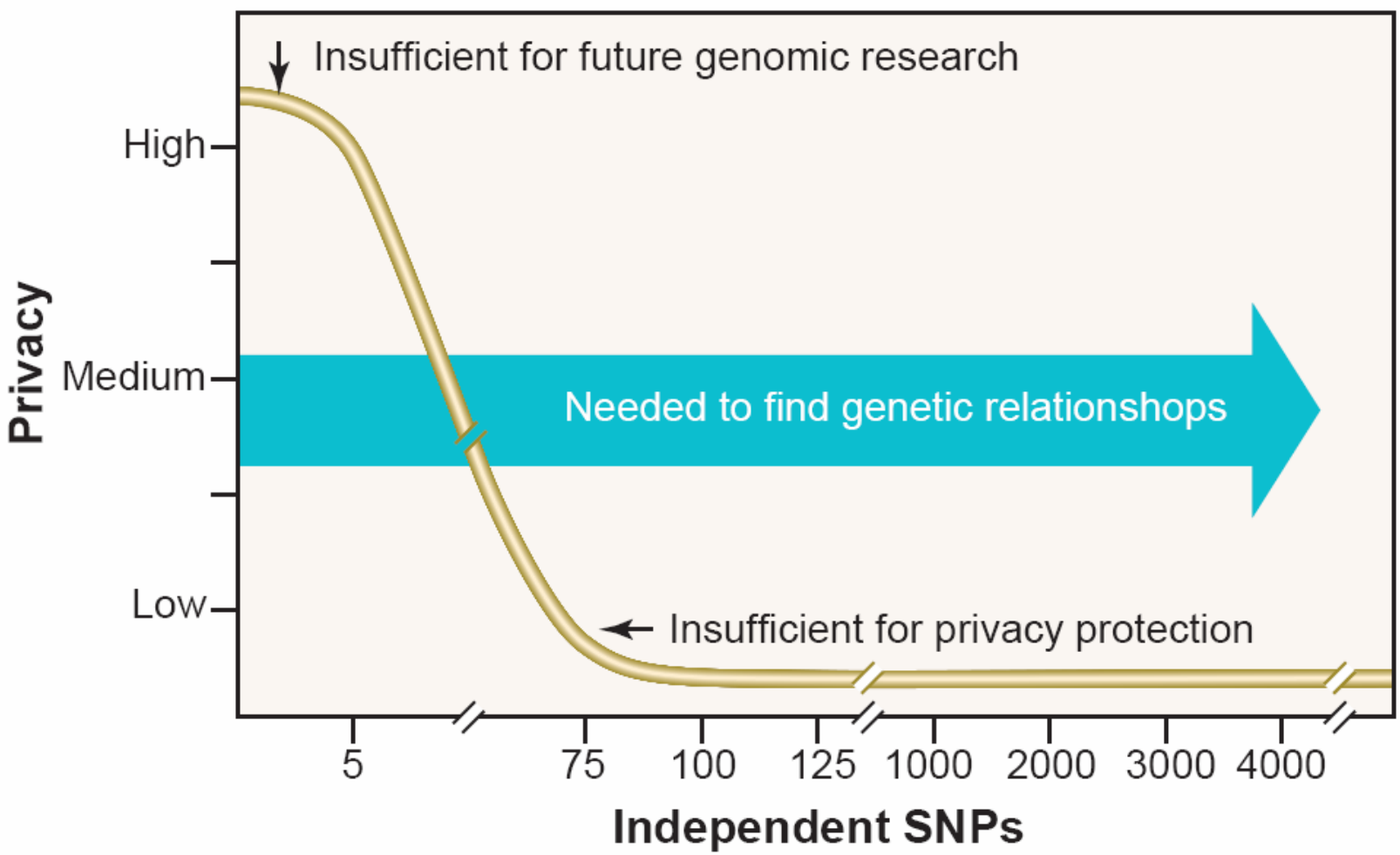
Microarray Data Transfer

Workflow | Array-Data | Database

Removed due to copyright reasons

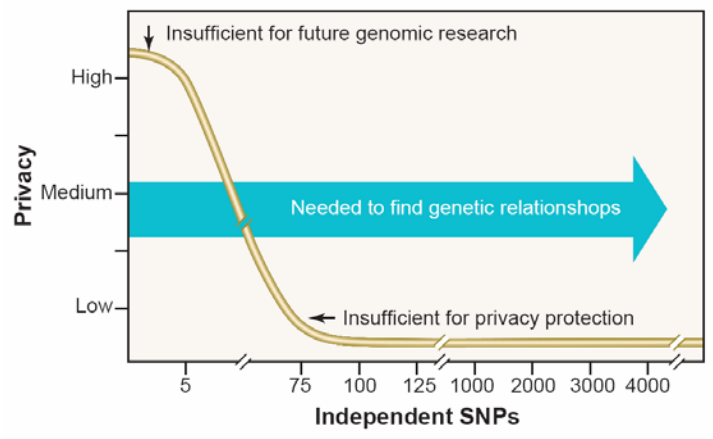
Courtesy: C. Lawerenz, NGFN

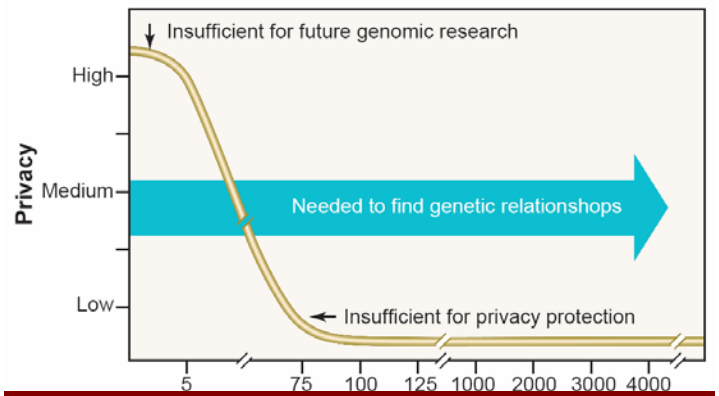
Example: Trade-offs between Single Nucleotide Polymorphisms (SNPs) and Privacy



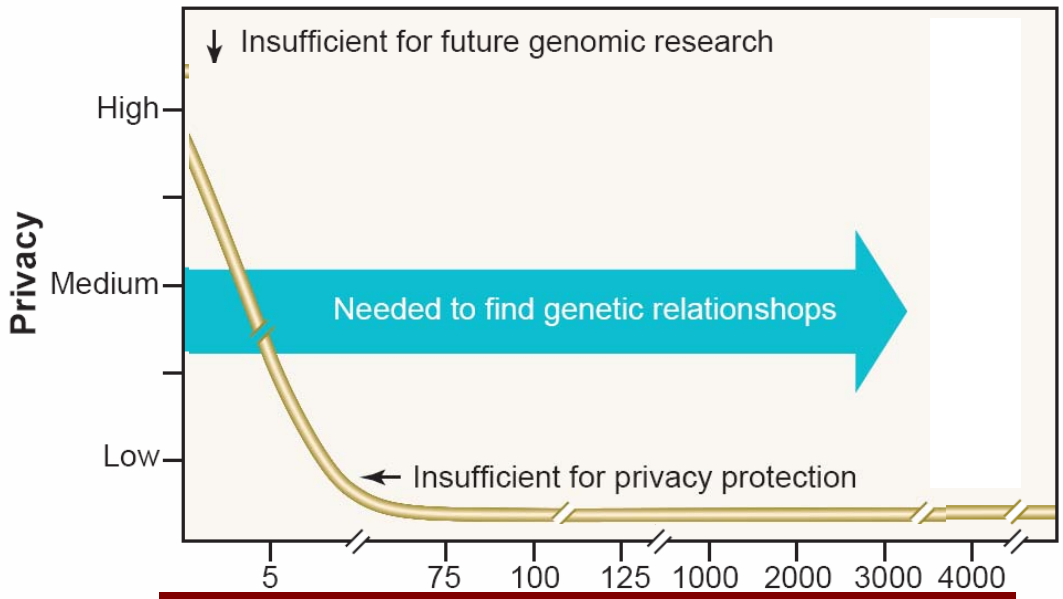
Lin Z, Owen AB, Altman RB. Science. Jul 9 2004;305(5681):183

Privacy concerns: Combination of data





Phenotype data



Combination of Genotype and Phenotype data

E) Privacy?!

Isaac Kohane (i2B2, Boston):

- **The cat is already out of the bag!**
- Most people are not fully aware of the degree to which their blood samples **can be and are used by the pharmaceutical industry**
- (When they learn, some wonder if they should participate in the profits that result from their samples)
- Insurance companies, hospitals **routinely share data** for reimbursement and research.

Genomic Privacy – possible solutions

- Competence networks have to be validated by TMF privacy WG and the federal Privacy Officers
- Privacy in Grid-Computing is a challenge

- Pseudonymization naïve de-identification do not suffice dealing with sequencing and SNP-data!
- K-Anonymity: each data set does not differ from k-1 other data sets (information loss!)
- Methods for giving **patient control of health data disclosure** could provide a mechanism for gathering research data (PHR)

Statistical Disclosure Control (SDC)

- **Microdata**: files with individual observations;
- **Tables**: total values carried by individuals
- **Other statistics** : summaries of different, indices, correlation coefficients, etc.
- → trade-off between the level of protection achieved for the data and the quality of the information released.
- **Information loss**:

- **How (not) to protect genomic data privacy in a distributed network: using trail re-identification to evaluate and design anonymity protection systems** *Journal of Biomedical Informatics, Volume 37, Issue 3, June 2004, Pages 179-192* Bradley Malin and Latanya Sweeney

Elements of Statistical Disclosure Control
Series: Lecture Notes in Statistics , Vol. 155
Willenborg, Leon, **Waal**, Ton de

Discussion

- Given the necessity to capture both environment and genomic state of a patient and their interaction, clinical information systems have to be redesigned.
- More integration work on terminologies and ontologies is to be done.
- Researchers from **medical informatics, bioinformatics and epidemiology** will have to **collaborate** much more intensively than they formerly did.
- One of the main problems may be the different vocabulary and the different background of these researchers.
- Sustainable collaborations would give German Biomedical Informatics a competitive edge in the community.

Take Home Message

- Genome wide association studies
  - ✓ genotyping constantly gets cheaper, phenotypic anotation drives the price!
- challenges
  - A) sufficient case numbers
  - B) high quality patient material to be genotype
  - C) high quality phenotype data
  - D) how can we homogenize the heterogeneous data sources
  - E) privacy problems!
- Researchers from **medical informatics, bioinformatics and epidemiology** will have to **collaborate** much more intensively

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