Introduction to Next Generation Sequencing

CGEpi Winter School 2017

Theory

- Wanted: DNA variations – difference to wildtype
- Evolution: Sanger technique 1977, Human Genome Projects 1990-2004
  - Ever cheaper NGS technologies, compete with microarrays
- Principles of Sequencing (Polymerase Chain Reaction –PCR)
  - DNA polymerase
  - Many PCR Cycles – DN.A amplification and signal measurement
- Several reads required
  - Very much data
  - Handling of errors
  - Shift from lab to computers

Practice

- NGS is only a technology – assays needed for practice
  - Whole genome
  - Exome
  - RNA expression, epigenome, amplicons, …
  - Many problems – starting with different methods (Sanger, Illumina (market leader))
- Reference genome - e.g. UCSC (e.g. hg38)
- Application in Galaxy software (usegalaxy.org)
  - Structure of data
  - quality check
  - Grooming, trimming and visualizing (cBioPortal) of data

Precision Oncology

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Gerstung et al 2016: Precision oncology for AML using a knowledge bank approach

Background

- Causative mutations drive the features of cancer and treatment response
- Considerable between-patient heterogeneity exists, limiting predictability

What to do?

Idea: use matched genomic-clinical data to support clinical decision making

Field: Acute myeloid leukemia (AML) – stem cell transplantation potential curative option but with strings attached

→Reanalyse data from 1540 AML patients

→Build multistage statistical model for prediction

→Validation by data from The Cancer Genome Atlas

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Outcome

- Personally tailored management could reduce the number of hematopoietic cell transplants by 20-25% with same OS
- However knowledge banks need information from number of patients