Genetics and genomics: Implications for clinical practice

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Network of Excellence EC-IST 2001-35024
Genetics and genomics are part of the genomic science

- Genetics identifies disease-related susceptibility genes
- Genomics identifies genes that belong to similar families based on their sequence homologies
- Genomic science is in the process of being integrated into the clinical setting
- The use of genomic science will help to profile variations between individuals’ DNA to improve diagnostic skills, determine prognosis and predict responses to environmental and behavioral factors, as well as responses to particular drugs
Transferring genomic science into a clinical setting is not easy

- Technical and cultural challenges will have to be conquered to be able to use the new powerful genetic research tools.
- These tools are now available to classify the heterogeneity of disease and the individual responses to drugs.
- Much of the genomic data of clinical relevance generated, has been stored in a format that is inappropriate for its use in routine diagnostic tests.
Many common diseases are multifactorial and polygenic.

- Stroke
- Breast cancer
- Myocardial Infarction
- Hypertension
- Diabetes
- Obesity
- Periodontitis
- Rheumatoid arthritis
- Inflammatory Bowel Diseases
- Psoriasis
WP 6.3 Genomics and chronic inflammation

Periodontitis and Biomedical Informatics

- Bioinformatics + Medical Informatics = Biomedical Informatics
- To discover and create novel diagnostic and therapeutic methods to improve of human health among others by the integration of genetic and clinical information with preventive, diagnostic and therapeutic purposes
- To set a long-lasting structure for the collaborative approach in Europe

The EC-funded INFOBIOMED Study (Network of Excellence EC-IST 2001-35024)
Infobiomed pilots

Pharmainformatics

Genomics and microbiology

Genomics and chronic inflammation (Periodontitis)

Genomics and colon cancer
Biomedical Informatics (BMI): an emerging discipline

- Medical Informatics has produced tools for medical and epidemiological research, patient care, and health management.
- Bio-Informatics has grown up with the Human Genome Project and handles genomics, proteomics and any other biological research data.
- BMI aims to make possible the necessary translation of multiple systems with different data bases into a common data base.

**clinical information and data analysis tasks**

**genomic information and data analysis tasks**
Periodontitis: An inflammatory, destructive disease of the supporting tissues of the teeth

- 10% of the total adult population suffers from severe periodontitis
- 30% of individuals >50 years (Brown et al 1990, Gjermo 1998)
Clinical signs of periodontitis

Host

Genetic factors
Systemic diseases
Smoking
Stress

P. gingivalis
A. actinomycetemcomitans
P. intermedia
T. forsythensis
P. micros
F. nucleatum

A multifactorial disease

Clinical signs of periodontitis
Periodontitis Data Warehouse

Enviromental data
Genomic data
Phenomic data
Microbiology data
Life habits data

Demographic data

Programs
Assessment / Annotation
External DBs

Periodontitis Data Warehouse
WP 6.3 Genomics and chronic inflammation

Integrate smoking data to the periodontitis database
• Definition of smoking
• Never, former or current smoker
• Age and time of quitting
• Number of cigarettes smoked per day for X years

Integrate microbial data to the periodontitis database
• Porphyromonas gingivalis
• Prevotella intermedia
• Tannerella forsythensis
• Fusobacterium nucleatum
• Actinobacillus actinomycetemcomitans
• Campylobacter rectus

Periodontitis Data Warehouse
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Periodontitis Data Warehouse
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To develop a life habits questionnaire and integrate it to the periodontitis database:
- Diet (Vitamins)
- Stress
- Hygiene
- Drugs prescription
- Socio-economisch status

Periodontitis Data Warehouse
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WP 6.3 Genomics and chronic inflammation

DIA tool (dental image analysis): ACTA & AVEIRO & UPM

INFOBIOMED Mobility funding - Luis Coelho, Aveiro, Portugal
Patients’ data storage model

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Privacy-enhanced data storage model
ACTA & Custodix & UPM

- PATIENTS
- ACTA
- Pseudonymous database at data warehouse
- Reversible encryption of identifiers (Name and date of birth)
- Specific record access (add/update/remove)
- Research community: VUMC, ACTA, others outside (statistical data processing)
Data Warehouse

- Environmental data
- Phenomic data
- Genomic data
- Microbiology data
- Life habits data
- Demographic data
- Assessment / Annotation
- External DBs
- Programs
Enabling BMI infrastructure

- Association Rule Mining (ARM): to identify interesting patterns and model profiles
- Decision Tree induction: to discriminate between classes of interest (e.g., healthy – not healthy)
- Clustering: to identify similarities across patient records and group similar records to clusters

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Data mining/visualization
1. Clustering
2. Classification
3. Association

Aims:
New classification of periodontitis
New clinico-genetic associations
New scientific hypotheses on pathophysiology of periodontitis
New insights/pathways in other complex chronic inflammatory diseases
Debt. of Periodontology
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Enabling technologies

Applications

MI
BMI
BI

FP6 EU Network of Excellence IST 2002-2006
GenePattern pipelines
http://www.broad.mit.edu/cancer/software/genepattern/

- At left is a diagrammatic representation of the computational method
- At right this set of steps in a single, reproducible pipeline that choreographs the entire process.

The pipeline is then available for modification, with each revision preserved for reproducibility and to share with colleagues and the community. Nature Genetics May 2006

Michael Reich, Ted Liefeld, Joshua Gould, Jim Lerner, Pablo Tamayo & Jill P Mesirov
Biomedical Informatics will make possible the necessary translation of multiple systems with different data bases into a common data base.

New comprehensive classification of inflammatory bowel disease

New clinico-genetic associations

New scientific hypotheses on pathophysiology of Crohn’s disease and ulcerative colitis

New insights/pathways in complex chronic inflammatory diseases