

Workshop on Cancer and Inflammation: Promise for Biological Therapy

Genetic Polymorphisms and Factors which Modulate Inflammation and Cancer

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Premises

- Chronic infection or inflammation lead to 20% of all human cancers
- Genetic variation controls expression of inflammatory genes
- The study of genetic variation offers an opportunity to understand pathogenesis and risk of cancer

Approaches to the study of host genetics

Candidate gene approach

Pathway analysis

Genome-wide association study

Markers

- Genetic markers that require functional validation
- Genetic markers that are population-specific
- By definition, may not be replicated in other populations

Gastric Cancer

- The recognized etiological factor is *H. pylori* infection
- Paradigm for inflammation-induced cancer
- Well-defined pre-cancer stages that constitute solid phenotypes
- Well-understood pathophysiology
- Easy to study host genetics

Gastric Cancer- Genetic Markers

- *IL1B*
- *IL1RN*
- *TNFA*
- *TLR4*
- *IL10*
- *IL8*
- *Others*

Gastric cancer – genetic markers

- Good for understanding pathogenesis but not ready as screening tools

Prostate cancer

- Innate immune genes (TLRs)
- *Propionibacterium acnes*

Prostate cancer - genetic association studies

- Definition of phenotype (case control status)
- Need more rigorous parameters for defining disease free individuals

Genome-wide association studies

- Technically becoming easier and affordable!!
- Require huge number of cases and controls with multi-stage design
- Several platforms are available (Affymetix and Illumina)
- Accepted significance level of 10^{-8}
- Cost 300-600 USD/person!!!

Host genetics – what is the value?

- Help to understand the pathophysiology of the disease
- May in due course define a genetic risk profile for screening
- The potential for understanding role of pharmacogenetics