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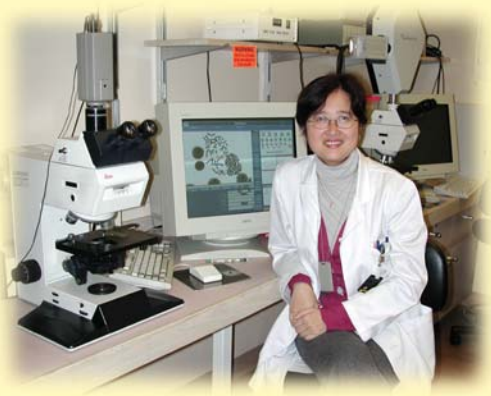
MOLECULAR PATHOLOGY Newsletter

Molecular Pathology Group, The Chinese University of Hong Kong

Clinical Cytogenetics Are Now Essential in the Management of Leukaemias

Dr Nathalie Wong



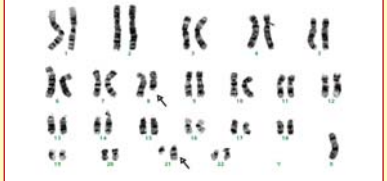
Clinical cytogenetics refer to the study of chromosome abnormalities in human diseases. Recurrent chromosomal translocations occur in more than half of all leukaemias and characterization of specific chromosomal rearrangements has provided useful information for diagnosis, prognostication, choice of therapy and follow-up monitoring in these patients. Cytogenetic analysis has now become a necessary workup of patients with leukaemia and related disorder such as the myelodysplastic syndrome. Recently, the Hospital Authority made cytogenetic and molecular cytogenetic tests part of its standard protocol for treatment of some leukaemias.

Traditionally, chromosomal morphology is visualised and karyotyped by G-banding techniques. With the advent of fluorescence-labelled DNA probes, it is now possible to utilise fluorescence-labelled probes in hybridization on chromosomes to determine specific abnormalities with accuracy. This technology of fluorescence in situ hybridization (FISH) is especially useful in detecting abnormalities beyond the resolution of G-banded chromosomes, and in determining the location of specific genes on chromosomes. There will be more on how molecular cytogenetics can be utilized in diagnostic situations in the next issue of this newsletter.

Chronic Myeloid Leukaemia (CML)

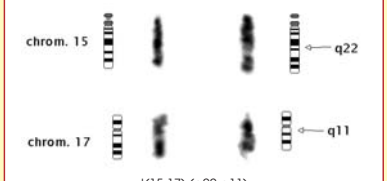
■ Almost all chronic phase CML patients exhibit a cytogenetic abnormality of translocation t(9;22) that results in the formation of Philadelphia chromosome (Ph). The identification of Ph translocation holds implication in the treatment therapy. "Gleevec" is an Abl-specific tyrosine kinase inhibitor that has marked activity in the treatment of CML and Ph chromosome-positive acute lymphoblastic leukaemia (ALL)

Acute Myeloid Leukaemia (AML: M2)



■ The t(8;21) rearrangement is almost exclusively observed in acute myeloid leukaemia (AML), especially AML: FAB M2. Additional chromosome changes are observed in over 75% of t(8;21) cases which include the loss of a sex chromosome. The presence of t(8;21) alone has been reported to suggest a good prognosis.

Acute Promyelocytic Leukaemia (APL: M3)



■ This translocation is remarkably specific for acute promyelocytic leukaemia (AML-M3). However, chromosomal analysis is often hampered by the suboptimal morphology. In cases of indefinable metaphase spreads, standard G-banding analysis can be difficult or even at times impossible. In such circumstances, supplementary FISH analysis has proven invaluable in establishing the presence of specific aberration.

Acute Myelomonocytic Leukaemia (AMMoL: M4eo)

■ Inversions of chromosome 16, and rearrangements involving band 16q22, are almost exclusively observed in acute myeloid leukaemia, specifically AMMoL: FAB-M4EO. This chromosome abnormality is associated with increased numbers of immature eosinophils in the bone marrow and peripheral blood. The inversion of chromosome 16, or a band 16q22 abnormality, is suggestive of a relatively good prognosis.

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Research News

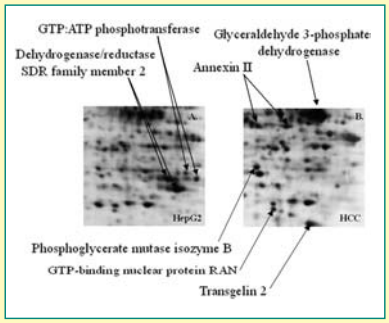
A New Tool for the Future : Proteomics, from Bench to Bedside

Dr Terence Poon

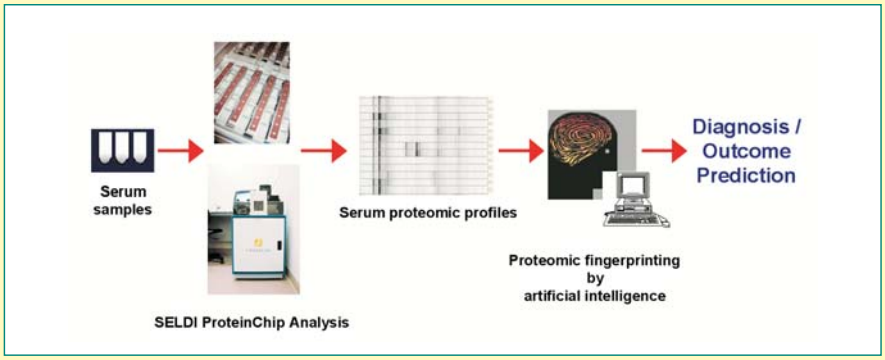
Proteins are functional products of genes. In the post-genome era, medical studies of global protein expression patterns and protein-protein interactions (i.e. Medical Proteomics) are important for understanding disease pathogenesis and development of diagnostic tools. We are carrying out various medical proteomic research projects, particularly in identifying new disease markers, and deciphering the global protein expression patterns of cancers.

Comparing the global protein expression patterns between cancer cells and normal cells can identify proteins playing important role in pathogenesis. Some of these abnormally regulated proteins can be used as molecular targets for new drug development while some can be used as new tissue markers for diagnosis, molecular classification or prognosis. With the support of a Central Allocation Grant from the University Grants Committee, one important project of our research team is identification of abnormally regulated proteins in liver cancer.

In order to develop non-invasive tools for disease diagnosis, prognosis, monitoring or outcome prediction, we use SELDI ProteinChip technology, a high-throughput technology to identify disease-specific proteomic fingerprints in blood. Recent data have indicated that specific serum proteomic fingerprints are present in various diseases, including liver cancer, liver fibrosis and severe acute respiratory syndrome. Validation translational studies are in process. In the future, these proteomic fingerprints can be applied to clinical practice.



■ By two-dimensional polyacrylamide gel electrophoresis and mass spectrometric analysis, proteins that are differentially expressed in hepatoblastoma cells (HepG2) and HCC cells are identified.



■ Application of serum protemic fingerprinting to disease diagnosis or outcome prediction.

Poon TCW, Hui AY, Chan HLY, et al. Prediction of liver fibrosis and cirrhosis in chronic hepatitis B infection by serum proteomic fingerprinting: a pilot study. *Clinical Chemistry* 51: 328-335, 2005

Pang TKR, Poon TCW, Wong N, et al. Comparison of Protein Expression Patterns between Hepatocellular Carcinoma Cell lines and a Hepatoblastoma Cell line. *Clinical Proteomics*. In press.

Dr Terence Poon, PhD, is Assistant Professor at the Department of Medicine and Therapeutics. His laboratory at the Cancer Centre, Faculty of Medicine, The Chinese University of Hong Kong, focuses on proteomic profiles of many diseases, especially cancers, and how they can be utilized in clinical situations.

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