conveyed by them may be much higher balancing the explained PAFs and FRRs (Hemminki et al PLOS ONE 2008;3:e2504).

623 Integrating biomarkers of exposure, risk and outcome in epidemiology

P. Boffetta[1]. [1]*Mount Sinai School of Medicine, Tisch Cancer Institute, New York, USA*

During the last two decades the use of biomarkers in cancer epidemiology has greatly increased. Several reasons explain this expansion. The identification of new carcinogens, characterized by complex exposure circumstances and weak effects, has become increasingly difficult with traditional epidemiological approaches. In parallel, increasing knowledge of mechanisms of carcinogenesis led to the proposal of models involving genetic and epigenetic events, as well as cellular and histological alterations. Furthermore, developments in molecular biology and genetics, such as the use of robots and the increasing throughput of automatic analytical equipments, allow the large-scale application of assays that would otherwise be very resource intensive.
A distinction has been made between markers of exposure, intermediate events, disease, outcome, and susceptibility. This distinction, however, is somewhat arbitrary, and any classification reflects the current understanding of a complex biological phenomenon such as carcinogenesis and the ability to measure events that are considered relevant to it. In fact, the increase in the understanding of the late steps in carcinogenesis, and the development of relevant and valid biomarkers, represents the main challenge to molecular cancer epidemiology.
If biomarkers are to offer new opportunities to overcome some of the limitations of epidemiology, then their added value over traditional approaches should be systematically assessed. Biomarkers should be validated and consideration of sources of bias and confounding in molecular epidemiology studies should be no less stringent than in other types of epidemiological studies. Similarly, other aspects of the study such as determination of required sample size, statistical analysis, reporting and interpretation of results should be approached with methodological rigor. One important goal is the integration of different types of biomarkers to derive risk and outcome profiles for healthy individuals as well as patients.

Tuesday 29 June 2010 12:20–13:45

Workshop: Grant opportunities

624 The role of the Marie Curie Actions in Cancer Research

E. Schermer[1], G. Wilkie[1]. [1]*European Commission, Marie Curie Host Fellowships, Brussels, Belgium*

Europe needs world-class research and world-class researchers, their creativity and skills. Our future depends critically on society's ability to inspire, motivate and train high quality researchers.
The European Commission's Marie Curie Actions scheme is a set of initiatives that aim to help researchers to fulfil their potential and develop their careers. The way that Marie Curie Actions work not only benefits the researcher themselves but also promotes research excellence and international collaboration, which bring benefits to society as a whole.
Marie Curie Actions promote the development and skills of researchers across Europe. The scheme helps researchers to broaden their career prospects, boosts the transfer of knowledge between researchers in different sectors and countries, and advances European excellence in research.
'Marie Curie Actions' follow a "bottom-up"-approach, hence they are open to researchers in any field of research, at all stages of their career and wherever they choose to do their research – in academia or industry.
During the session an overview of all funding schemes will be given and the role of the Marie Curie Actions in Cancer Research will be presented.
More information:
http://ec.europa.eu/research/mariecurieactions/

625 Not available

No abstract received.

Tuesday 29 June 2010 12:20–13:45

Workshop: Women in Science

626-627 Progress and promise

No abstract received.

Tuesday 29 June 2010 13:45–14:35

Plenary Lecture: AICR Lecture

628 The microenvironment and the genome in breast cancer: how tissue architecture informs

M. Bissell[1]. [1]*Lawrence Berkeley National Laboratory, Life Sciences Division, Berkeley, USA*

That development, differentiation and cancer are fundamentally connected has been appreciated for decades. How and why, however, still need much exploration. In the last three decades, we have developed a number of concepts and assays to study how a normal mammary gland conducts the processes of forming, branching, producing milk proteins, remodeling and maintaining steady-state and homeostasis. We have modeled the formation of the unit structure of the mammary gland, a polar 'acinus', and have followed the consequences of loss of its structural integrity. We show myoepithelial cells are crucial regulators of homeostasis and functional differentiation by their ability to make laminin111 (Ln-1) an extracellular matrix molecule (ECM) essential for formation of the acini, homeostasis and functional differentiation; both Ln1 and myoepithelial cells are virtually lost in breast cancer. We have evidence to show that the mechanisms that maintain polarity of the acini are important in preventing cancer, and the restoration of the unit structure can 'reverse' malignant progression.
In the last decade, we have used some of these concepts to understand also the nature of the breast stem and precursor niche. Further more, taking a leaf from invasion and branching of the normal gland in virgin mice, we have developed new models and techniques for understanding invasion and metastasis. Finally, such models have helped us define the plasticity of both normal and malignant cells and the possibility of using microenvironmental therapies to treat breast and other forms of cancer.

Tuesday 29 June 2010 14:35–16:35

Symposium

Cancer stem cells

629 The molecular portraits of breast cancer and their relationship to mammary stem cells

C. Perou[1]. [1]*University of North Carolina at Chapel Hill, Chapel Hill, USA*

Background: Breast cancer is a heterogeneous disease in terms of histology, dissemination patterns, therapeutic responses, and patient outcomes. Gene expression analyses using DNA microarrays have helped to explain some of this heterogeneity and provided important new clues as to the cellular origins of many breast tumours.
Material and Methods: Genomic studies using DNA microarrays have established five major breast cancer intrinsic subtypes (Luminal A, Luminal B, HER2-enriched, Claudin-low, Basal-like) and a Normal Breast-like group. FACS analysis of normal human mammary epithelial cells, mouse models, and cell lines, have identified a mammary luminal cell developmental pathway starting from a bi-potent stem cell, to a luminal progenitor, and ending in a mature ER+ luminal cell.
Results: We compared the genomic profiles of each intrinsic subtype to that of profiles coming from FACS isolated mammary epithelial cell populations in order to determine if any relationships might exist. We also present the most recent therapeutic data on the intrinsic subtypes of breast cancer with a special focus on the Claudin-low subtype; this unique subtype shows many mesenchymal and stem cell-associated features, and by genomic analyses it appears to be the most related to the bi-potent normal mammary stem cell fraction. In addition, recent evidence also suggests that the typically triple-negative Basal-like tumour subtype may represent a committed luminal progenitor, with the Luminal A/B tumours showing a mature luminal cell profile.
Conclusion: The observed intrinsic subtypes of breast cancer appear to mimic normal mammary development with each subtype representing a distinct stage of development. These findings also have important implications for the potential cell type of transformation of each subtype, which may be a stem cell for some subtypes (Claudin-low and Basal-like) and a differentiated cell for others (Luminal A).

630 Prospective cloning of functionally distinct breast cancer cells by use of markers from a normal human breast lineage hierarchy

O. Petersen[1]. [1]*The Panum Institute, Structural Cell Biology Unit, Institute of Medical Anatomy, Copenhagen, Denmark*

Tumour heterogeneity is a hallmark of cancer and it is responsible for tumour progression and resistance to therapy. According to Nowell's classical theory