EMERGING ROLE OF NOVEL MOLECULAR SUBTYPES TO PREDICT COLORECTAL CANCER CLINICAL OUTCOME

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Consensus molecular subtyping (CMS) is currently the most robust classifier for colorectal cancer (CRC) based on gene expression profiling, with accumulating evidence that these subtypes may also predict response to treatment and clinical outcome. Recently we have also used copy number alterations (CNAs) of CRC samples and subsequent unsupervised clustering to classify metastatic CRC tumours as a subtype triumvirate relating patients' response to bevacizumab plus chemotherapy and outcome. Tumours that are classified in clusters 2 and 3 (CMS2 and 4) show additional benefit from bevacizumab treatment when compared to patients from the same cluster that received chemotherapy only. Hyper-mutator phenotypes, such as tumours with POLE or POLD1 mutations or micro-satellite instable tumours show no additional benefit from bevacizumab treatment and importantly also microsatellite stable tumours with a stable copy number profile show no additional benefit from bevacizumab treatment. We therefore propose that chromosomal instability represents a novel biomarker for bevacizumab response. Tumours with a high proportion of the genome affected by CNAs have a significantly better response when treated with bevacizumab compared to copy number stable tumours. Novel CRC molecular sub-typing approaches are now poised to impact clinical treatment paradigms.

Biography

Annette Byrne is currently an Associate Professor (Physiology) and Head of the Laboratory for Tumour Biology and Molecular Imaging (LTBMI) at the Royal College of Surgeons in Ireland gained a PhD in Cell Biology at the University of York, UK, She was awarded the John Kerner fellowship in Gynaecologic Oncology from the University of California, San Francisco. During this period she was engaged in the elucidation of novel angiogenesis targets involved in the development of ovarian cancer, as well as interrogating the *in vivo* activity of novel therapeutics. Subsequently, She was recruited as Scientist by Pharmacyclics LLC (Sunnyvale, California) to investigate the mechanism of action of a new class of radiation/ chemotherapy under clinical development. In 2003 she relocated to New York where she was employed as Senior Scientist in Angion Biomedica Corp, whose main focus was developing therapeutics which manipulated angiogenesis signaling pathways. Prof Byrne returned to Ireland in 2005 to the position of Principal Investigator at University College Dublin's Conway Institute. During this engagement she was instrumental in establishing Ireland's first comprehensive Tumour Xenograft Facility and translational Pre-clinical Imaging Centre. Prof Byrne was recruited to the Royal College of Surgeons in Ireland in 2008 as tenured Lecturer (Physiology) and Principal Investigator, RCSI Centre for Systems Medicine & Dept of Physiology and Medical Physics. Prof Byrne was promoted to Snr Lecturer in 2013 and to Associate Professor in 2017.

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