

Seminar series FOR2127 – Selection and adaptation during metastatic cancer progression

Thursday, 25 October 2018

University Hospital A2, Kursraum 1
14.00 h



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“Epigenomics and Epitranscriptomics in Human Disease: From Knowledge to Applications”

An altered pattern of epigenetic modifications is central to many common human diseases, including cancer. Many studies have explored the mosaic patterns of DNA methylation and histone modifications in cancer cells on a gene-by-gene basis, among them the seminal finding of transcriptional silencing of tumor suppressor genes by CpG island promoter hypermethylation. Epigenetic gene inactivation in transformed cells involves many “belts of silencing”. We are in the process of completing the molecular dissection of the entire epigenetic machinery involved in methylation-associated silencing, such as DNA methyltransferases, methyl-CpG binding domain proteins, histone deacetylases, histone methyltransferases, histone demethylases and Polycomb proteins. The first indications are also starting to emerge about how the combination of cellular selection and targeted pathways leads to abnormal DNA methylation. In addition to classical tumor-suppressor and DNA repair genes, epigenetic gene silencing includes microRNAs with growth inhibitory functions. Recent technological advances are now enabling cancer epigenetics to be studied genome-wide. It is time to “upgrade” cancer epigenetics research and put together an ambitious plan to tackle the many unanswered questions in this field using genomics approaches to unravel the epigenome.

Selected reading:

Moran S, Martínez-Cardús A, Sayols S, Musulén E, Balañá C, Estival-Gonzalez A, Moutinho C, Heyn H, Diaz-Lagares A, de Moura MC, Stella GM, Comoglio PM, Ruiz-Miró M, Matias-Guiu X, Pazo-Cid R, Antón A, Lopez-Lopez R, Soler G, Longo F, Guerra I, Fernandez S, Assenov Y, Plass C, Morales R, Carles J, Bowtell D, Mileschkin L, Sia D, Tothill R, Tabernero J, Llovet JM, Esteller M. Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis. *Lancet Oncol.* 2016 Oct;17(10):1386-1395. doi: 10.1016/S1470-2045(16)30297-2. Epub 2016 Aug 27. PubMed PMID: 27575023.

Perez-Salvia M, Aldaba E, Vara Y, Fabre M, Ferrer C, Masdeu C, Zubia A, San Sebastian E, Otaegui D, Llinàs-Arias P, Rosselló-Tortella M, Berdasco M, Moutinho C, Setien F, Villanueva A, González-Barca E, Muncunill J, Navarro JT, Piris MA, Cossio FP, Esteller M. In vitro and in vivo activity of a new small-molecule inhibitor of HDAC6 in mantle cell lymphoma. *Haematologica.* 2018 Jun 7. pii: haematol.2018.189241. doi: 10.3324/haematol.2018.189241. [Epub ahead of print] PubMed PMID: 29880608.