Publications de l’équipe
Génomique et biologie des cancers du sein héréditaires

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The biological and prognostic significance of angiotropism in uveal melanoma.
Laboratory investigation; a journal of technical methods and pathology : DOI:
10.1038/labinvest.2017.16

Résumé

Angiotropism is a marker of extravascular migration of melanoma cells along vascular and other structures and a prognostic factor in cutaneous melanoma. Because of this biological and prognostic importance in cutaneous melanoma, angiotropism was studied in uveal melanoma (UM). This retrospective study performed at a single ocular oncology referral center included 89 patients from the study period 2006-2008. All patients were diagnosed with UM from the choroid and/or ciliary body. All patients underwent enucleation for prognostic purposes and definitive therapy. Clinical, histopathological, and molecular variables included patient age, gender, extraocular extension, tumor location (ciliary body or not), optic nerve invasion, angiotropism, neurotropism, melanoma cell type, BAP1 mutation, and monosomy 3. Angiotropism was defined as melanoma cells arrayed along the abluminal vascular surfaces without intravasation in the sclera and/or episcleral tissue. The study included 51 women (57.3%) and 38 men with mean and median age: 63 years (range: 25-92). Mean follow-up was 4.4 years (range: 0.2 to 11). Fifty-three (59.6%) patients developed metastases and 48 (53.9%) were dead from metastases at last follow-up. Other principal variables recorded were angiotropism in 43.8%, extraocular extension in 7.9%, epithelioid/mixed cell type in 73.1%, BAP1 mutation in 41.3%, and monosomy 3 in 53.6% of cases. On multivariate analysis, extraocular extension, angiotropism, and monosomy 3 were predictive of metastasis, whereas tumor diameter, epithelioid cell type, angiotropism, and monosomy 3 were predictive of death. Chi-square test confirmed an association between angiotropism and metastasis and death but none with BAP1 mutation and monosomy 3. In conclusion, angiotropism and monosomy 3 were independent prognostic factors for both metastases and death in UM. However, irrespective of any prognostic value, the true importance of angiotropism is its biological significance as a marker of an alternative metastatic pathway.

Francesca Riva, Francois-Clement Bidard, Alexandre Houy, Adrien Saliou, Jordan Madic, Aurore Rampanou, Caroline Hego, Maud Milder, Paul Cottu, Marie-Paule Sablin, Anne Vincent-Salomon, Olivier Lantz, Marc-Henri Stern, Charlotte Proudhon, Jean-Yves Pierga (2017 Jan 12)

Patient-Specific Circulating Tumor DNA Detection during Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer.
Clinical chemistry : DOI : clinchem.2016.262337
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Résumé

In nonmetastatic triple-negative breast cancer (TNBC) patients, we investigated whether circulating tumor DNA (ctDNA) detection can reflect the tumor response to neoadjuvant chemotherapy (NCT) and detect minimal residual disease after surgery.

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Francesca Riva, Oleksii I Dronov, Dmytro I Khomenko, Florence Huguet, Christophe Louvet, Pascale Mariani, Marc-Henri Stern, Olivier Lantz, Charlotte Proudhon, Jean-Yves Pierga, Francois-Clement Bidard (2016 Feb 10)

Clinical applications of circulating tumor DNA and circulating tumor cells in pancreatic cancer.
Molecular oncology : 481-93 : DOI : 10.1016/j.molonc.2016.01.006

Résumé

Pancreatic ductal adenocarcinoma (PDAC) is the most frequent pancreatic cancer type and is characterized by a dismal prognosis due to late diagnosis, local tumor invasion, frequent distant metastases and poor sensitivity to current therapy. In this context, circulating tumor cells and circulating tumor DNA constitute easily accessible blood-borne tumor biomarkers that may prove their clinical interest for screening, early diagnosis and metastatic risk assessment of PDAC. Moreover these markers represent a tool to assess PDAC mutational landscape. In this review, together with key biological findings, we summarize the clinical results obtained using « liquid biopsies » at the different stages of the disease, for early and metastatic diagnosis as well as monitoring during therapy.

Tatiana Popova, Elodie Manié, Valentina Boeva, Aude Battistella, Oumou Goundiam, Nicholas K Smith, Christopher R Mueller, Virginie Raynal, Odette Mariani, Xavier Sastre-Garau, Marc-Henri Stern (2016 Jan 21)

Ovarian Cancers Harboring Inactivating Mutations in CDK12 Display a Distinct Genomic Instability Pattern Characterized by Large Tandem Duplications.
Cancer research : 1882-91 : DOI : 10.1158/0008-5472.CAN-15-2128

Résumé

CDK12 is a recurrently mutated gene in serous ovarian carcinoma, whose downregulation is associated with impaired expression of DNA damage repair genes and subsequent hypersensitivity to DNA-damaging agents and PARP1/2 inhibitors. In this study, we investigated the genomic landscape associated with CDK12 inactivation in patients with serous ovarian carcinoma. We show that CDK12 loss was consistently associated with a particular genomic instability pattern characterized by hundreds of tandem duplications of up to 10 megabases (Mb) in size. Tandem duplications were characterized by a bimodal
(~0.3 and ~3 Mb) size distribution and overlapping microhomology at the breakpoints. This genomic instability, denoted as the CDK12 TD-plus phenotype, is remarkably distinct from other alteration patterns described in breast and ovarian cancers. The CDK12 TD-plus phenotype was associated with a greater than 10% gain in genomic content and occurred at a 3% to 4% rate in The Cancer Genome Atlas-derived and in-house cohorts of patients with serous ovarian carcinoma. Moreover, CDK12-inactivating mutations together with the TD-plus phenotype were also observed in prostate cancers. Our finding provides new insight toward deciphering the function of CDK12 in genome maintenance and oncogenesis. Cancer Res; 76(7); 1882-91. ©2016 AACR.