

## **The impact of cellular senescence and DNA damage on colorectal tumour progression**

Helen Angell, Marie Tosolini, Bernhard Mlecnik, Gabriela Bindea, Tessa Fredriksen, Lucie Lafontaine, Maximilian Waldner, Franck Pagès, Viia Valge-Archer, Jérôme Galon

► **To cite this version:**

Helen Angell, Marie Tosolini, Bernhard Mlecnik, Gabriela Bindea, Tessa Fredriksen, et al.. The impact of cellular senescence and DNA damage on colorectal tumour progression. *Journal for Immunotherapy of Cancer*, BMJ Publishing Group 2013, 1 (Suppl 1), pp.P144. inserm-00881033

**HAL Id: inserm-00881033**

**<https://www.hal.inserm.fr/inserm-00881033>**

Submitted on 7 Nov 2013

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**POSTER PRESENTATION**

**Open Access**

# The impact of cellular senescence and DNA damage on colorectal tumour progression

Helen K Angell<sup>1,2,3\*</sup>, Marie Tosolini<sup>1,2,3</sup>, Bernhard Mlecnik<sup>1,2,3</sup>, Gabriela Bindea<sup>1,2,3</sup>, Tessa Fredriksen<sup>1,2,3</sup>, Lucie Lafontaine<sup>1,2,3</sup>, Maximilian Waldner<sup>1,3,4</sup>, Franck Pagès<sup>1,3,5</sup>, Vija Valge-Archer<sup>6</sup>, Jérôme Galon<sup>1,2,3</sup>

From Society for Immunotherapy of Cancer 28th Annual Meeting  
National Harbor, MD, USA. 8-10 November 2013

We have previously defined the immune contexture as the type, density, location and functional orientation of tumour infiltrating immune cells, associated with patient prognosis in colorectal cancer (CRC). Here we describe potential mechanisms, including the DNA damage response (DDR) and cellular senescence, as contributing factors in shaping this intra-tumoural immune reaction. Cellular senescence, permanent proliferation arrest, is triggered by exogenous or endogenous stress, including telomere shortening, DNA-damage or oncogene activation. We have evaluated the expression of 53BP1, pATM and p16INK4a in a cohort of 205 CRC patients. In addition, telomere length and senescence-associated  $\beta$ -galactosidase have been analysed. A large panel of immune markers, including CD3, CD45RO, CD8 and CD57, were evaluated immunohistochemically. Patients who had increased DDR and senescence correlated with improved prognosis, both disease free and overall survival. Patients with high 53BP1 and pATM had significantly higher numbers of infiltrating immune cells at both the tumour centre and invasive margin. Functional experiments, including a transwell chemotaxis system, have illustrated that immune cells migrate towards soluble factors produced by senescent tumour cells. Our data provide further mechanisms resulting in changes of specific immune cell densities within the tumour, illustrating links between senescence and aspects of the DDR with the control of the anti-tumour immune response, and thus CRC disease progression.

#### Authors' details

<sup>1</sup>Laboratory of Integrative Cancer Immunology, INSERM U872, Paris, France.

<sup>2</sup>Université Paris Descartes, Paris, France. <sup>3</sup>Cordeliers Research Centre,

<sup>1</sup>Laboratory of Integrative Cancer Immunology, INSERM U872, Paris, France  
Full list of author information is available at the end of the article

Université Pierre et Marie Curie Paris 6, Paris, France. <sup>4</sup>University of Erlangen-Nuremberg, Erlangen, Germany. <sup>5</sup>Immunology, Georges Pompidou European Hospital, Paris, France. <sup>6</sup>MedImmune Ltd, Cambridge, UK.

Published: 7 November 2013

doi:10.1186/2051-1426-1-S1-P144

**Cite this article as:** Angell et al.: The impact of cellular senescence and DNA damage on colorectal tumour progression. *Journal for ImmunoTherapy of Cancer* 2013 **1**(Suppl 1):P144.

**Submit your next manuscript to BioMed Central  
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
[www.biomedcentral.com/submit](http://www.biomedcentral.com/submit)

