University of Birmingham

Professor Tatjana Stankovic MD, PhD

Professor in Cancer Genetics

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About

Tatjana Stankovic is a Professor in Cancer Genetics.

Tatjana Stankovic has published over 60 research papers in high impact scientific journals as well as reviews in the fields of cancer genetics and DNA damage response. She has received grants from the Leukaemia Research Fund, Cancer Research UK , Kay Kendall Leukaemia Fund, and CLIC.

She is an enthusiastic advocator of translational cancer research and gives frequent talks at both local and national meetings.

Qualifications

- 2010-present Professor in Cancer Genetics, School of Cancer Sciences, University of Birmingham
- 1990-2010 Research Fellow, Senior Lecturer, Reader at the CRUK Institute for Cancer Studies, University of Birmingham
- 1982-1989 House officer, Paediatrician, Lecturer at the University of Belgrade (Children's Hospital)

Biography

Tatjana Stankovic completed her Medical Degree, Master's Degree in Haematology and training in Paediatrics at the University of Belgrade. She joined the University of Birmingham in 1990 where she completed her PhD studies on the cloning of the gene for Ataxia Telangiectasia in 1995.

Since 2000, Tanja Stankovic is running her own research group. The emphasis of her research is on a strong network of highly productive local, national and international collaborations and a clear focus on translational implementation of scientific findings related to the role of DNA damage response in pathogenesis and therapeutic response of haematopoetic malignancies. This includes research on Ataxia Telangiectasia Mutated (ATM) gene in chronic lymphocutic leukaemia and other ATM null lymphoid malignancies, the role of kinase deregulation in damage response in paediatric leukaemia and significance of chromatin modifying agents in therapeutic response of myeloid leukaemias. The ultimate goal is translation of basic research into clinical trials which is supported by development of xenograft models for all major types of lymphoid malignancies.

Teaching

Teaching Programmes

Professor Stankovic is a strong believer in significance of teaching excellence. She is taking an active part in the annual assessment of individual PhD student progress, interviews with individual students with their supervisors and providing advice on student progress where required.

- She is a member of the School and College Learning/Teaching Committee with particular responsibilities for the BMedSc year 3 option on 'Cancer pathogenesis and treatment' an MSc (Clinical Oncology) module on 'Paediatric oncology'
- She teaches MBChB undergraduates the BMedSc undergraduate course (years 1, 2 and 3) MSc (Clinical Oncology)
- She regularly supervises research projects for both MBChB intercalating students and also BMedSc students.

Postgraduate supervision

Professor Stankovic is interested in supervising doctoral research students in the following areas:

- The role of DNA damage response in generation of genomic instability in haematopoietic malignancies
- The deregulation of DNA damage response pathways in sporadic cancers as a tool for targeted treatment

If you are interesting in studying any of these subject areas please contact Prof Stankovic on the contact details above, or for any general doctoral research enquiries, please email: **dr@contacts.bham.ac.uk (mailto:dr@contacts.bham.ac.uk)** or call +44 (0)121 414 5005.

For a full list of available Doctoral Research opportunities, please visit our Doctoral Research programme listings.

Research

Research Themes

Cancer Cell Biology, Clinical Trials, DNA damage response and genomic instability

Research Activity

ATM-dependent pathways as therapeutic targets in CLL

The pleiotropic nature of the ATM mutant CLL cellular phenotype provides multiple ways for sensitisation of ATM mutant tumours. This concept is called synthetic lethality. For example, the current hypothesis is that inhibition of DNA repair pathways that cooperate with ATM could sensitize ATM mutant cells by a mechanism that

does not involve activation of apoptosis. This lead to the use of a novel, highly specific PARP inhibitor (olaparib) that is already in the phase I/II clinical trials for BRCA mutant tumours in ATM null lymphoid malignancies. The group has shown that ATM null tumour cells show sensitivity to PARP inhibitor both in vitro and in vivo in an ATM null xenograft model. Based on multicentre national collaboration a phase I/II clinical trial with PARP inhibitor in ATM null lymphoid malignancies has been initiated.

Development of murine models for ATM deficient lymphoid malignancies

The mechanisms by which loss of ATM function can promote malignancies at different stages of haematopoietic differentiation are largely unknown. Furthermore, lack of animal models severely hampers the comprehensive development of targeted treatments for these aggressive malignancies. Therefore, an important recent task was to produce an Atm-/- mouse model in which early thymoma development is blocked and the full range of ATM driven haematopoietic malignancies can be recapitulated. To facilitate this task a series of crosses of Atm-/+ heterozygous mice with nude mice lacking a thymus due to loss of the Foxn1 alleles has been undertaken. Atm-/-nu-/- double knockout animals lacking a T cell compartment, display a prolonged median survival time, delayed tumour onset and a change in tumour phenotype towards diffuse large B-cell -like lymphomas (DLBCL) as well as myeloproliferation. This provides an excellent model to study the role of ATM in a wide range of malignancies. Finally, xenografts for all major leukaemias have been developed to facilitate testing of targeted therapies.

Targeting DNA damage response in paediatric ALL

The aim is to design the best strategies of targeting pro-survival pathways that confer apoptosis resistance in ALL. To facilitate this aim the group has undertaken a wide screen of kinome and DNA repair profiles and identified deregulated kinases and DNA repair proteins associated with apoptosis resistance. These proteins will be targeted by pharmacological inhibitors. Leukaemia xenograft models will provide a unique tool to monitor the response of a leukaemia stem cell population in apoptosis resistant leukaemias to any treatment that targets deregulated proteins.

Other activities

Member of:

- UK-CLL forum Executive Committee
- European Research Initiative on CLL (ERIC)
- Scientific Committee of the International Workshop on ‘Ataxia Telangiectasia/ATM’
- Childhood Leukaemia Research UK (CLR-UK)

Publications

Pepper C, Lin TT, Pratt G, Hewamana S, Brennan P, Hiller L, Hills R, Ward R, Starczynski J, Austen B, Hooper L, Stankovic T, Fegan C. (2008) Mcl-1 expression has in vitro and in vivo significance in chronic lymphocytic leukemia and is associated with other poor prognostic markers. Blood;112:3807-17

Marston E, Weston V, Jesson J, Maina E, McConville C, Agathanggelou A, Skowronska A, Mapp K, Sameith K, Powell JE, Lawson S, Kearns P, Falciani F, Taylor M, Stankovic T. (2009) Stratification of paediatric ALL by in vitro cellular responses to DNA double strand breaks provides insight into the molecular mechanisms underlying clinical response Blood. 113(1):117-26.

Sameith K, Antczak P, Marston E, Turan N, Maier D, Stankovic T, Falciani F. (2008) Functional Modules integrating essential cellular functions are predictive of the response of leukaemia cells to DNA damage. Bioinformatics. 24:2602-7.

Bose S, Yap LF, Fung M, Starzcynski J, Saleh A, Morgan S, Dawson C, Chukwuma MB, Maina E, Buettner M, Wei W, Arrand J, Lim PVH, Young LS, Teo SH, Stankovic T, Woodman CBJ, Murray PG. (2009) The ATM tumour suppressor gene is downregulated in EBV-associated nasopharyngeal carcinoma. J Pathology (3):345-52.

Stewart GS, Panier S, Townsend K, Al-Hakim A, Kolas NK, Miller ES, Nakada S, Ylanko J, Olivarius S, Mendez M, Tagliaferro A, Pelletier L, Taubenheim N, Durandy A, Byrd PJ, Stankovic T, Taylor AMR, Durocher D. (2009) The gene mutated in the RIDDLE syndrome regulates an ubiquitin-dependent signalling cascade at sites of DNA damage. Cell; 136:420-34.

Dunwell TL, Dickinson RE, Stankovic T, Dallol A, Weston V, Austen B, Catchpoole D, Maher ER, Latif F.Frequent epigenetic inactivation of the SLIT2 gene in chronic and acute lymphocytic leukemia. Epigenetics. 2009 May;4(4):265-69.

Goodyear O, Agathanggelou A, Novitzky-Basso I, Siddique S, McSkeane T, Ryann G, Vyas P, Cavenagh J, Stankovic T, Moss P, Craddock C. (2010) Induction of a CTL Response to the MAGE Cancer Testis Antigen by Combined Treatment with Azacitidine and Sodium Valproate in Patients with Acute Myeloid Leukemia and Myelodysplasia. Blood;116(11):1908-18.

Weston VJ, Oldreive CE, Skowronska A, Oscier DG, Pratt G, Dyer MJS, Smith G, Powell JE, Taylor AMR, Moss PAH, Stankovic T (2010). The PARP inhibitor olaparib suppresses growth of ATM mutant lymphoid tumour cells in vitro and in vivo. Blood;116(22):4578-87