Cluster of Excellence
- "From Regenerative Biology to Reconstructive Therapy"

Lunch Seminar

Guest:

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„Genetic fate mapping of cancer stem cells in myelodysplastic syndrome patients"

Tuesday, February 3, 2015

Seminar Room of the Institute of Human Genetics
Theoretische Institute II (Bldg. I6)
Level 01, Room 2013, 12:00 s.t.

To arrange an appointment with the guest, please contact:
Secretarial Office - Prof. Dr. B. Schlegelberger, Tel. 0511 532-4523

Genetic fate mapping of cancer stem cells in myelodysplastic syndrome patients

Experimental evidence supporting the existence of human cancer stem cells (CSCs) remain extensively contested and in vivo fate mapping of candidate human CSCs in patients has not been possible. Through establishment of molecularly and functionally distinct and hierarchically organized stem and progenitor cell compartments in myelodysplastic syndromes (MDS) and backtracking of identified somatic genetic lesions, we establish that rare Lin-CD34+CD38-CD90+CD45RA- MDS cells function as MDS-propagating cells in patients with low- to intermediate-risk MDS. Because their elimination will be essential, and possibly also sufficient, towards eradication of the entire MDS clone, the definitive identification of rare but distinct MDS stem cells will now facilitate development of therapies specifically targeting MDS stem cells.

Relevant publications:

- **Woll PS**, Kjällquist K, Chowdhury O, Doolittle D, Wedge DC, Thongjuea S, Erlandsson R, Ngara M, Anderson K, Deng Q, Mead AJ, Stenson L, Giustacchini A, Duarte S, Giannoulatou E, Taylor S, Karimi M, Scharenberg C, Mortera-Blanco T, Macaulay IC, Clark S-A, Dybedal I, Josefsen D, Fenaux P, Hokland P, Holm MS, Cazzola M, Malcovati L, Tauro S, Bowen D, Boultwood J, Pellagatti A, Pimanda JE, Unnikrishnan A, Vyas P, Göhring G, Schlegelberger B, Tobiasson M, Kvalheim G, Constantinescu SN, Nerlov C, Nilsson L, Campbell PJ, Sandberg R, Papaemmanuil E, Hellström-Lindberg E, Linnarsson S, Jacobsen SEW. Myelodysplastic syndromes are propagated by rare and distinct human cancer stem cells in vivo. *Cancer Cell* 2014, 25:794-808.
- Bardini M, **Woll PS**, Corral L, Luc S, Wittman L, Ma Z, Nigro LL, Basso G, Biondi A, Cazzaniga G, Jacobsen SEW. Clonal variegation and dynamic competition of leukemia-initiating cells in infant acute lymphoblastic leukemia with MLL rearrangement. *Leukemia* 2014, doi: 10.1038/leu.2014.154.
- Böiers C, Carrelha J, Lutteropp M, Luc S, Green JC, Azzoni E, **Woll PS**, Mead AJ, Hultquist A, Swiers G, Perdiguero EG, Macaulay IC, Melchiori L, Luis TC, Kharazi S, Bouriez-Jones T, Deng Q, Pontén A, Atkinson D, Jensen CT, Sitnicka E, Geissmann F, Godin I, Sandberg R, de Bruijn MF, Jacobsen SE. Lymphomyeloid contribution of an immune-restricted progenitor emerging prior to definitive hematopoietic stem cells. *Cell Stem Cell* 2013, 13:535-48.
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- Lutz C, **Woll PS**, Hall G, Castor A, Dreau H, Cazzaniga G, Zuna J, Jensen C, Clark SA, Biondi A, Mitchell C, Ferry H, Schuh A, Buckle V, Jacobsen SE, Enver T. Quiescent leukemia cells account for minimal residual disease in childhood lymphoblastic leukemia. *Leukemia* 2013, 27:1204-7.

- Luc S, Luis TC, Boukarabila H, Macaulay IC, Buza-Vidas N, Bouriez-Jones T, Lutteropp M, **Woll PS**, Loughran SJ, Mead AJ, Hultquist A, Brown J, Mizukami T, Matsuoka S, Ferry H, Anderson K, Duarte S, Atkinson D, Soneji S, Domanski A, Farley A, Sanjuan-Pla A, Carella C, Patient R, de Bruijn M, Enver T, Nerlov C, Blackburn C, Godin I, Jacobsen SE. The earliest thymic T cell progenitors sustain B cell and myeloid lineage potential. *Nat Immunol* 2012, 13: 412-419.
- Buza-Vidas N, **Woll P**, Hultquist A, Duarte S, Lutteropp M, Bouriez-Jones T, Ferry H, Luc S, Jacobsen SE. FLT3 expression initiates in fully multipotent mouse hematopoietic progenitor cells. *Blood* 2011, 118: 1544-1548.
- Tehranchi R*, **Woll PS***, Anderson K*, Buza-Vidas N, Mizukami T, Mead AJ, Astrand-Grundström I, Strömbeck B, Horvat A, Ferry H, Dhanda RS, Hast R, Rydén T, Vyas P, Göhring G, Schlegelberger B, Johansson B, Hellström-Lindberg E, List A, Nilsson L, Jacobsen SE. Persistent malignant stem cells in del(5q) myelodysplasia in remission. *N Engl J Med* 2010, 363:1025-1037. (*These authors contributed equally to this article)
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- **Woll PS**, Morris J, Painschab, M, Marcus R, Kohn A, Biechele T, Moon R, Kaufman DS: Canonical Wnt signaling promotes hemato-endothelial cell development from human embryonic stem cells. *Blood* 2008, 111:122-131.
- **Woll PS**, Martin CH, Miller JS, Kaufman DS: Human embryonic stem cell-derived NK cells acquire functional receptors and cytolytic activity. *J Immunol* 2005, 175:5095-5103.