Dear All,

A warm welcome to the seminar "***In situ* tumor arrays reveal early environmental control of cancer immunity"** by Dr. Christine Moussion (Genentech) on **Friday the 24th of March at 11.15 AM** in Biomedicum lecture hall 3.

The seminar is organized by Translational Cancer Medicine Research Program (CAN-PRO) and iCAN Digital Precision Cancer Medicine Flagship.

Recent breakthroughs have emphasized the key role of patients' immune defense in designing efficient tumor-targeting therapies. Despite the remarkable successes, the current remedies are efficient only for a subset of patients, highlighting the urgent need to better understand the evolution of anti-tumor immune responses. Dr. Christine Moussion will present a novel preclinical approach, which aims at resolving the mechanisms of microenvironmental control that dictate the outcome of the anti-tumor responses (*Nature* in press).

Contact the host Dr. Kari Vaahtomeri (kari.vaahtomeri@helsinki) for an appointment with the speaker.

Follow the seminar via zoom:
https://helsinki.zoom.us/j/64804986682?pwd=ME8rOVhucnQ5YXE1VVdpck5BN25BZz09

Meeting ID: 648 0498 6682
Passcode: 366409

Abstract:
The immune phenotype of a tumor is a key predictor of its response to immunotherapy. Patients who respond to checkpoint blockade generally present with 'immune-inflamed' tumors highly infiltrated by T cells. However, not all inflamed tumors respond to therapy, and even lower response rates occur among tumors that lack T cells ('immune-desert') or that spatially exclude T cells to the periphery of the tumor lesion ('immune-excluded'). Despite the importance of these tumor immune phenotypes in patients, little is known about their development, heterogeneity or dynamics due to the technical difficulty of tracking these features *in situ*. Here, we introduce STAMP (*S*kin *T*umor *A*rray by *M*icro*P*oration), a novel preclinical approach that combines high-throughput time-lapse imaging with next-generation sequencing of tumor arrays. Using STAMP, we followed the development of thousands of arrayed tumors *in vivo* to show that tumor immune phenotypes and outcomes vary between adjacent tumors and are controlled by local factors within the tumor microenvironment. More particularly, the recruitment of T cells by fibroblasts and monocytes into the tumor core was supportive of T cell cytotoxic activity and tumor rejection. Importantly tumor immune phenotypes were dynamic over-time and an early conversion to an 'immune-inflamed' phenotype was predictive of spontaneous or therapy-induced tumor rejection. Thus, STAMP captures the dynamic

relationships of spatial, cellular and molecular components of tumor rejection and has the potential to translate novel therapeutic concepts into successful clinical strategies.

Biography:

Dr. Moussion received her PhD from the University of Toulouse (France) where she studied the mechanisms controlling the migration of lymphocytes from blood to tissues in the lab of Jean-Philippe Girard at IPBS. She then moved to IST Austria in Vienna as a Postdoctoral fellow in the group of Michael Sixt to study mechanisms controlling Dendritic cells (DCs) migration from the periphery to the draining lymph node through the lymphatic circulation. In 2016, Dr. Moussion joined Genentech (San Francisco, CA) as a team leader in the Cancer Immunology Department. Her group bridges basic science and drug discovery by deciphering and targeting novel cellular and molecular mechanisms that limit the recruitment of leukocytes in the context of an anti-tumor Immune response. By combining innovative high throughput in vivo imaging technologies with genetic and pharmacological tools, her group pursues discoveries of novel biological pathways from mouse models to human pathology, to improve the outcome of Immunotherapies in the treatment of solid tumors.

Selected Publications:

- FLT3L-Fc NG2LH, a new player for Cancer Immunotherapy combinations. Decalf.J, Toy.E, He.D, Kenkre.K, Berkley.A, Kwong.M, Kee.Y, Sun.Y, Wang.X, Myneni.S, Ebtikar.A, Ancheta.A, Yang.Y, Kim.H, Tang.N, Banerji.D, Mai.E, Dogra.P, Phung.W, Day.P, Sandoval.W, Meric.O, Chan.P, Sanjabi.S, Comps-Agrar.L, Cohen.S, Ernst.J, Liu.Y, Lazar.G, Hosseini.I, Kemball.C, Schartner.J, Bainbridge.T*, **Moussion.C*.** *Under review at ebioMedicine.*

- *In situ* tumor arrays reveal early environmental control of cancer immunity Ortiz-Muñoz.G*, Brown.M*, Carbone.C*, Pechuan-Jorge. X*, Rouilly.V, Lindberg.H, Ritter.A, Raghupathi.G, Sun.Q, Nicotra.T, Mantri.S, Yang.A, Doerr.J, Nagarkar.D, Darmanis.S, Haley.B, Mariathasan.S, Wang.Y, Gomez-Roca.C, de Andrea.C, Spigel.D, Wu.T, Delamarre.L, Schöneberg.J, Modrusan.Z, Price.R, Turley.S, Mellman.I, **Moussion.C**. *In press Nature 2023.*

- Lineage tracing reveals the unique pro-tumorigenic niche role of tissue-resident macrophages in early cancer lesions. Casanova-Acebes.M, Dalla.E, Leader.A, LeBerichel.J, Nikolic.J, Morales.B, Brown.M, Chang.C, Troncoso.L, Chen.S, Sastre-Perona.A, Park.M, Tabachnikova.A, Dhainaut.M, Hamon.P, Maier.B, Sawai.C, Agulló-Pascual.E, Schober.M, Brown.B, Reizis.B, Kenigsberg.E, **Moussion.C**, Benaroch.P, Aguirre-Ghiso.J, Merad.M. *Nature, Jul;595(7868):578-584 (2021)*

- Gremlin 1+ 1 fibroblastic niche maintains dendritic cell homeostasis in lymphoid tissues Kapoor.V, Müller.S, Keerthivasan.S, Brown.M, Chalouni.C, Storm.E, Castiglioni.A, Lane.R, Nitschcke.M, Dominguez.C, Astarita.J, Krishnamurty.A, Carbone.C, Senbabaoglu.Y, Wang.A, Wu.X, Cremasco.V, Roose-Girma.M, Tam.L, Doerr.J, Chen.M, Lee.W, Modrusan.Z, Yang.A, Bourgon.R, Sandoval.W, Shaw.A, De Sauvage.F, Mellman.I, **Christine Moussion**, Shannon J. Turley. *Nature Immunology, 22(5):571-585 (2021)*

- The Dendritic Cell Strikes Back. **Moussion C**, Mellman I. Immunity. 2018 Dec 18;49(6):997-999.

- Tumour lymph vessels boost immunotherapy. **Moussion C**, Turley SJ. Nature. 2017 Dec21; 552(7685):340-342.

- Polysialylation of CCR7 controls dendritic cell trafficking by releasing CCL21 from an auto-inhibited state. Kiermaier E*, **Moussion C***, Veldkamp C, Gerardy-Schahn R, Williams L, Chaffee G, Phillips A, Freiberger F, Imre R, Taleski D, Payne R, Mechtler K, Mühlenhoff M, Volkman B, Sixt M. *Science.* 351: 86-190 (Jan 2016).

- Interstitial dendritic cell guidance by haptotactic chemokine gradients. Weber M, Hauschild R, Schwarz J, **Moussion C**, de Vries I, Legler DF, Luther SA, Bollenbach T, Sixt M. *Science.* 339: 328-32 (2013).

- HEVs, lymphatics and homeostatic immune cell trafficking in lymph nodes. Girard JP, **Moussion C**, Förster R. *Nat Rev Immunol.* 12: 762-73 (2012).

- Dendritic cells control lymphocytes entry to lymph node through high endothelial venules. **Moussion. C** and Girard JP. *Nature*. 479: 542-546 (2011).

- Anti-inflammatory effects of an inflammatory chemokine: CCL2 inhibits lymphocyte homing by modulation of CCL21 triggered integrin-mediated adhesions Flaishon L*, Hart G*, Einat Zelman*, **Moussion C***, Grabovsky V, Lapidot T, Feigelson S, Margalit R, Harmelin A, Avin T, Shoseyov D, Alon R, Girard JP and Shachar I. *Blood* 112: 5016-5025 (2008).

- The IL-1 like cytokine IL-33 is constitutively expressed in the nucleus of endothelial cells and epithelial cells *in vivo*: A novel alarmin? **Moussion C***, Ortega N* and Girard JP. *PLoS ONE* 3(10): e3331 (2008) *(>1200 citations)*