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# The Auckland Cancer Research Network

**Friday 20th November 2015**

**11am-12pm**

**Lecture theatre 503-024, FMHS, Grafton**

## Prof Antonio Bertoletti, MD

**“Cellular Immune Therapies for HBV chronic infection and related liver tumor”**

**Abstract:**

Cancer immunotherapy using a patient’s own T cells redirected to recognize and kill tumor cells has achieved promising results in metastatic melanoma and leukemia. This technique involves harnessing a patient’s T cells and then delivering a gene that encodes a new T cell receptor or a chimeric antigen receptor that allow the cells to recognize specific cancer antigens. The potential for development of redirected T cell therapy for persistent viral infections like HBV and their associated malignancies has started to be explored by different groups and we recently demonstrated in a first-in-man clinical trial that the adoptive transfer of HBV-specific TCR redirected T cells in a patient with HBsAg-productive hepatocellularcarcinoma (HCC) targeted the cancerous cells and caused a profound inhibition of HBsAg production. However, adoptive T cell therapy for CHB is still regarded with skepticism because HBV-specific T cells can potentially attack infected hepatocytes that are not cancerous, possibly leading to severe liver damage. The challenge to design TCR redirected T cells that can cure virally infected cells without damaging the normal liver is open. We will discuss new concepts and methods that might lead to the clinical use of TCR redirected T cells in HBV-related HCC or chronic HBV infection.

**Antonio Bertoletti, M.D.**

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| **Antonio Bertoletti, M.D.**  Professor,  Duke-NUS Medical School  Division Emerging Infectious Diseases,  Singapore  Tel: + 65 66013574  Fax: + 65 6772 4112  Email: [antonio@duke-nus.edu.sg](mailto:antonio@duke-nus.edu.sg)  Skype: bertolettiaa | Description: ::::::::::::Pictures:Antonio. Antonio Bertoletti:Primo piano .jpg |

**Antonio Bertoletti, MD** is an expert in the field of viral hepatitis. He began working in viral hepatitis as a medical student at the University of Parma (Italy). During his MD specialization (1991) in Infectious Diseases he spent two years at The Scripps Research Institute (La Jolla) characterizing for the first time in human the *Hepatitis B virus* (HBV) specific cytotoxic T cells. He returned to the University of Parma, where he worked in the Department of Infectious Diseases as a Clinical Scientist continuing his study of human HBV specific T cells (1991-1997). before joining “The UCL Institute of Hepatology” at University College of London (UK) (1997).

In 2006 he moved to Singapore where he was the Director of Infection and Immunity Program at the Singapore Institute for Clinical Sciences (A\*STAR) until 2013 before moving in 2013 at the Emerging Viral Disease Program at Duke-NUS Medical School.

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**Research Interests:**

immunopathogenesis of HBV infection. His current research is focus on understanding the impact of age in HBV infection/pathology and on the development of new immunological based therapies (TCR-redirected T cells, HLA-peptide specific antibodies) for the treatment of HBV and Hepatocellularcarcinoma.

**Selected Publications:**

1. AJ Gehring, M Haniffa, P Kennedy, Z Z Ho, C Boni, A Shin, N Banu, SG Lim, A Chia, C Ferrari, F Ginhoux, A Bertoletti**.** Mobilizing Monocytes to Cross-present Circulating Viral Antigen in Chronic Infection. 2013 **J Clin Invest**. 123(9):3766-76.
2. Jo J, Tan AT Ussher JE, Sandalova E,Tang XZ, , Natalie To, Hong , Chia A, Gill US, Kennedy PT, Tan KC, Lee KH, De Libero G, Gehring AJ, Willberg CB, Klenerman P, Bertoletti A. TLR8 agonist and bacteria trigger a potent activation of innate immune cells resident in human liver.**. 2014 Plos Pathog.** doi/10.1371/journal.ppat.1004210
3. Immunotherapy of HCC metastases with autologous T cell receptor redirected T cells targeting HBsAg in a liver transplant patient.Qasim W, Brunetto M, Gehring A, Xue SA, Schurich A, Khakpoor A, Zhan H, Ciccorossi P, Gilmour K, Cavallone D, Moriconi F, Farzhenah F, Mazzoni A, Chan L, Morris E, Thrasher A, Maini M, Bonino F, Stauss H, Bertoletti A.**J Hepatol. 2015** 62:468-91
4. Hong, M., Sandalova, E., Low, D., Gehring, A. J., Fieni, S., Amadei, B., Urbani S., Chop Y.S., Guccione E, Bertoletti A Trained immunity in newborn infants of HBV-infected mothers. **Nature Communications 2015** , *6*, 1–12. doi:10.1038/ncomms7588.
5. Pallett, L. J., Gill, U. S., Quaglia, A., Sinclair, L. V., Jover-Cobos, M., Schurich, A., Singh KP, Thomas N, Das A, Chen A, Fusai G, Bertoletti A, Cantrell D, Kennedy PTF, Davies N, Haniffa MA, Maini MK.. (2015). Metabolic regulation of hepatitis B immunopathology by myeloid-derived suppressor cells. ***Nature Med. 2015***, 21: 591-560.