International Joint Usage/Research Center Seminar

Subject: **Searching for T cell exhaustion modifiers**

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Date: **Wednesday,Jan 29,2020**

Time: **2:00pm-3:30pm**

Venue: **Building.1**

2-1 conference room

Host:

Prof.Ken J. Ishii

Division of Vaccine Science

Abstract:

Exhaustion is a dysfunctional state of cytotoxic CD8+ T cells (CTL) that is observed in chronic infection and cancer. The success of immune checkpoint inhibition in cancer immunotherapy relies on the blocking the continuous negative signalling that exhausted cells receive by inhibitory receptors such as PD-1 and CTLA-4. Identifying therefore modulators of CTL exhaustion is expected to provide therapeutic benefit. We have embarked on a quest to identify small molecules that can reverse or prevent CTL exhaustion. Because in vivo models of CTL exhaustion yield very few exhausted CTL and the in vivo inflammatory milieu in these models can obscure the phenotype of exhausted CTL, we have developed an in vitro system to induce bona fide CTL exhaustion. Using this system, we have identified small molecules that can modify exhaustion and prevent or restore key features of CTL exhaustion. This in vitro system can be used to identify genes and signalling pathways involved in exhaustion and facilitate the screening of reagents that prevent/reverse CTL exhaustion. Such molecules can be used alone or in combination with other immunotherapies in cancer and chronic infections.

Publication list:

J. Immunol. 183:5006-12, 2009, ***Vaccine*** 29:314-322, 2010, ***J. Immunol.*** 186:4599-4608, 2011, ***PLOS Pathogens*** 7: e1002055, 2011 , ***Blood*** 118: 2520-9, 2011, ***Nat Immunol.*** 14:593-602, 2013, ***PLOS Pathogens*** 9: e1003658, 2013, ***J. Immunol.*** 196:1186-98, 2016, ***J. Immunol.*** 196:2602-13, 2016, ***Front. Immunol.*** 8:1696, 2017, ***Front. Immunol.*** 8:1859, 2017, ***Front. Immunol.*** 9:446, 2018 , ***J. Virol.*** 92(21). pii: e01325-18, 2018.