**Engineered immune cells as highly sensitive cancer diagnostics**

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**Presenter**: Shih-Min Chen **Date/Time**: 2020/03/12, 15:10-16:00

**Commentator**: Nan-Haw Chow, M.D. **Location:** Room 601, Med College Building

**Background**

 Early detection of primary disease is one of the most promising approaches to reducing the growing cancer burden. So far, endogenous biomarkers remain at the front line of early disease detection, but many lack the sensitivities and specificities necessary to influence disease management. An alternative diagnostic strategy is the systemic delivery of probes with selective promoters that can be activated and generate signals in the presence of a protease-rich disease environment. It can improve sensitivities and signal-to-noise ratios but limited by biocompatibility of the probe, efficient delivery to sites of pathology. Leverage metabolic alterations occurring in tumor-infiltrating immune cells and describe cellular sensors for highly sensitive cancer detection.

**Objective/Hypothesis**

 To engineer macrophages to produce a synthetic reporter by coupling luciferase expression to activation of the arginase-1 promoter, that allowing homing to sites of disease and subsequently image the host and detected by bioluminescence imaging and luciferase measured in the blood which may be a potential immune cell sensor for early disease detection.

**Results**

 M2 macrophages are the predominant immune cells in most solid tumors from the iPRECOG dataset. The author selected macrophages as a pan-cancer diagnostic sensor candidate. *Arg1* is upregulated by stimulation of IL-4, IL-3 and TCM in both endogenous and adoptively transferred tumor-infiltrating murine macrophages. Also, the adoptively transferred macrophages migrate to and accumulate in TMEs. By engineering macrophages, the activation of *Arg1* would be coupled to production of secreted luciferase that can detected tumors as small as 25–50 mm3 by blood luciferase measurements and exhibit greater sensitivity than existing cancer biomarkers. Additionally, the macrophage sensorsalso effectively tracked the immunological response in muscle and lung models of inflammation.

**Conclusion**

 The engineered macrophages demonstrate a biocompatible and potentially generalizable immune cell sensor for early disease detection.

**References**

Colegio, O. R. et al. Functional polarization of tumour-associated macrophages by tumour-derived lactic acid. *Nature* **513**, 559–563 (2014).