黃玄舜 助理研究員 Dr. Huang, Hsuan-Shun

E-mail：san.sam@msa.hinet.net

分機：17660

Tzu Chi University, Taiwan. Ph.D.

專長：Molecular Oncology, Immunoregulation

研究興趣：

高級別漿液性卵巢癌的成因不明，多在晚期才發現，為死亡率最高的女性特有癌症。隨著全球工業化社會轉型、人口老化、女性少育、晚婚等因素，卵巢癌的威脅逐年上升成為婦科最大死因。我們以臨床檢體及分子細胞生物技術為基礎，在先前的研究已發現排卵濾泡液的自由基及經血倒流的血紅素為致癌初始因子與協助因子，目前正一步步釐清濾泡液中致癌驅化因子，從分子層面，試圖拼出卵巢癌形成模式。本系列研究除了增進癌症病因學的發展外，更重要的是希望能提供卵巢癌初級預防及次級預防的重要資訊，以期減緩現代婦女遭受此疾病的威脅

The current research in our team focuses on the etiology of ovarian cancer. This cancer is the fifth leading cause of death of female cancer worldwide. The five-year mortality rate is 60% and the vast majority of deaths are from the histology type of high-grade serous ovarian carcinoma (HGSC) [high-grade means poorly differentiated], accounting for the number one killer of gynecological cancers. The poor prognosis of ovarian HGSC is mainly due to the elusive etiology and the lack of early symptoms or signs for diagnosis. The recent breakthrough findings indicate that fallopian tube fimbriae are the real origin of ovarian HGSC and incessant ovulation is a major risk. Fallopian tube fimbriae approach ovulatory follicle and pick the oocytes after ovulation. We speculated that there might be some carcinogens in the ovulating follicular fluid (FF) that initiate the transformation of fimbria epithelium.

We have established in vitro, in vivo and ex vivo models to recapitulate many of the ovulating effects on fallopian tube fimbriae. These include HPV E6/E7-immortalized human fimbrial epithelial cell line (FE25), ex vivo-cultured human and mouse fimbria tissue as well as Tp53-null transgenic mice, each exposed to human FF aspirates and its carcinogenic components. We have discovered two cancer initiation culprits of fimbria carcinogenesis, conferring the original etiology of ovarian HGSC: ROS in ovulatory FF was the main mutagen that can cause DNA double strand break (DSB) of fimbrial epithelial

cells and hemoglobin from retrograde menstruation was the auxiliary surviving factor that alleviated the NOX1-mediated cell apoptosis under the oxidative and DNA damaged stress. However, only these two factors cannot fully transform immortalized cells, there are other unknown carcinogens required to be discovered. I continue to investigate the ovulation-induced carcinogenesis of fallopian tube epithelium. I hope, by using the clinical specimens-based in vitro and in vivo research models, we will achieve a clear picture of the transformation process of ovulation-induced fimbral carcinogenesis, and pave ways to primary and secondary prevention of ovarian HGSC.

成果發表(5 年內)：

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