FSH 所引起的 Sertoli cell 快速外鈣引入的分子機制，及其所活化的轉錄因子之探討

Study on the molecular mechanisms of FSH-induced immediate Ca2+-influx and subsequent transcription factor activation in rat Sertoli cells

中文摘要

科學界一向深信促濾泡成長激素(FSH)會刺激史托利細胞(Sertoli cell)經由一連串與 Gs/cAMP 有關的訊息傳遞路徑而影響基因的表現。另一方面， Sertoli cell 受到 FSH 刺激之後，也會引起外鈣引入(Ca2+ influx)。本實驗室的研究結果和其他報導皆證實此一外鈣引入的訊息傳遞路徑與 Gs/cAMP 無關，但是與磷酸脂?C (phospholipase C)有關。基於以上的報導，在本研究中我們更進一步證實此外鈣引流路徑爲 Gah/PLCd1，另外我們又致力於探討大白鼠(rat)的 Sertoli cell，因 FSH 引發之快速鈣引流路徑所調控之轉錄因子 AP-1 的活化情況。

本研究成果證實了 FSH 所引發的外鈣引入現象是在 FSH 與 “FSH receptor” 結合之後，活化 Gah，進而活化 PLCd1，此訊號繼續下傳而引進細胞外的鈣離子。同時我們也發現，以 FSH 處理 Sertoli 細胞 10 分鐘會活化 AP-1，此活化現象至少維持到 FSH 作用 60 分鐘，而以作用 30 分鐘的組別 AP-1 由細胞質轉位到細胞核內的效應最好。同時我們也證實，這些轉錄因子之轉位及活化的確經由 Gah-PLCd1 之訊號傳遞路徑所調控，這些研究成果使我們對 FSH 調控 Sertoli cell 部份 功能的分子機制有了更深入的了解。

英文摘要

It is well accepted that follicle-stimulating hormone (FSH) interacts with its receptor on Sertoli cells and elicits a cascade of biochemical events preceded by the activation of Gs/adenylate cyclase pathway. On the other hand, the action of FSH on Sertoli cells also induces an extracellular calcium influx. Our previous study and others demonstrated that this event was Gs/cAMP independent, but phospholipase C dependent. In this study, we demonstrated that FSH-induced Ca++-influx of Sertoli cells was mediated by Gah/PLCd1 signaling pathway. Efforts were further made to identify the involvement of Gah/PLCd1 pathway in FSH-induced AP-1 activation. The data showed that upon FSH-FSH receptor binding, the signal activated Gah within seconds. The activated Gah interacted with PLCd1 and modulated the subsequent FSH-induced Ca2+-influx of rat Sertoli cells in a dose-dependent manner. Moreover, the interaction of FSH with Sertoli cells caused AP-1 activation, the effect occurred from 10 minutes to 60 minutes of FSH treatment. The maximal response was

observed at 30 minutes of FSH-inclusion in the culture media. These results, it is concluded that Gah-PLCd1 pathway indeed mediated the FSH-induced Ca++-influx, and subsequent AP-1 activation and translocation.