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**Major Professor:** Colin Jefcoate

**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** B.S Genetic Engineering, Suwon University, M.S Bacteriology, Univ Wisconsin-Madison

**Current Research Project:**

The steroidogenic acute regulatory protein (StAR) is generated in rodents from 1.6kb and 3.5kb mRNA formed by alternative polyadenylation. The zinc finger protein, TIS11B (also Znf36L1), is elevated by cAMP in adrenal cells in parallel with StAR mRNA. TIS11b selectively destabilizes the 3.5kb mRNA through AU-rich sequences at the end of the 3'UTR. siRNA suppression shows that TIS11b surprisingly increases StAR protein and cholesterol metabolism. StAR transcription is directly activated by PKA phosphorylation. cAMP responsive element binding protein 1 (CREB) phosphorylation is a key step leading to recruitment of the co-activator, CREB binding protein (CBP). A second protein, CREB regulated transcription coactivator (TORC/CRTC), enhances this recruitment, but is inhibited by Salt inducible kinase (SIK). Basal StAR transcription is constrained through this phosphorylation of TORC. PKA provides an alternative stimulation by phosphorylating SIK, which prevents TORC inactivation. PKA stimulation of StAR nuclear transcripts substantially precedes TORC recruitment to the StAR promoter, which may, therefore, mediate a later step in mRNA production. Inhibition of SIK by staurosporine elevates StAR transcription and TORC recruitment to maximum levels, but without CREB phosphorylation. TORC suppression by SIK evidently limits basal StAR transcription. Staurosporine and cAMP stimulate synergistically. SIK targets the phosphatase, PP2a (activation), and Type2 histone de-acetylases (inhibition), which may each contribute to suppression. Staurosporine stimulation through SIK inhibition is repeated in cAMP stimulation of many steroidogenic genes regulated by steroidogenic factor 1 (SF-1) and CREB. TIS11b and SIK may combine to attenuate StAR expression when hormonal stimuli decline.

**Honors:**

**Grants Received:**

**Publications:**

Jefcoate CR, Lee J, Cherradi N, Takemori H and Duan H. cAMP stimulation of STAR expression and cholesterol metabolism is modulated by co-expression of labile suppressors of transcription and mRNA turnover. *Molecular and Cellular Endocrinology*. 2010. In Press.

**National Presentations:**



Jinwoo Lee and Colin Jefcoate. Superoxide generation and oxidative stress in the regulation of StAR expression. The adrenal cortex and molecular steroidogenesis conference 2008,

Jinwoo Lee, Haichuan Duan and Colin Jefcoate. Synergy Between PKA and PKC Stimulation of StAR Expression: Evidence for Distinct Nuclear Pathways Controlled by Acetylation/De-acetylation. The adrenal cortex and molecular steroidogenesis conference 2010

## **Other Presentations:**

Jinwoo Lee and Colin Jefcoate. Synergy between PKA and PKC Stimulation of StAR Expression: Evidence for Distinct Nuclear Pathways Controlled by Acetylation/De-acetylation. ERP Annual Symposium 2008.

Jinwoo Lee and Colin Jefcoate. Superoxide generation and oxidative stress in the regulation of StAR expression. ERP Annual Symposium 2009.

Jinwoo Lee and Colin Jefcoate. Regulation of Steroidogenic Acute Regulatory (stAR) Gene By Protein Kinase A (PKA) and Salt Inducible Kinase (SIK). Annual Symposium 2010.

## **ERP Service:**

Seminar Committee