

# **Isolation and Properties of Gas 8, a Growth-Arrest-Specific Gene Regulated during Male Gametogenesis to Produce a Protein Associated with the Sperm Motility Apparatus.**

李文森

Shauh-Der Yeh;Ying-Jiun Chen;Annie C. Y. Chang;Rabindranath Ray;Bin-Ru She;Wen-Sen Lee;Han-Sun Chiang;Stanley N. Cohen;and Sue Lin-Shao.

## **Abstract**

Growth arrest-specific (Gas) genes are expressed during serum starvation or contact inhibition of cells grown in culture. Here we report the isolation and characterization of Gas8, a novel gene identified on the basis of its growth arrest-specific expression in murine fibroblasts. We show that production of Gas8 mRNA and protein occurs in adult mice predominantly in the testes, where expression is regulated during postmeiotic development of male gametocytes. Whereas a low level of Gas8 mRNA was detected by Northern blotting in testes of murine male neonates and young adolescents, Gas8 mRNA increased rapidly postmeiotically. In adult males, both Gas8 mRNA and protein reached steady state levels in testes that were 10-fold higher than in other tissues. Immunohistochemical analyses showed that Gas8 protein accumulates in gametocytes as they approach the lumen of seminiferous tubules and is localized to the cytoplasm of round spermatids, the tails of elongating spermatids, and mature spermatid tail bundles protruding into the lumen; in epididymal spermatozoa Gas8 protein was present in the flagella. However, premeiotic murine gametocytes lacked detectable Gas8 protein, as did seminiferous tubules in biopsy specimens from seven human males having cytological evidence of non-obstructive azoospermia secondary to Sertoli cell-only syndrome. Our findings, which associate Gas8 production developmentally with the later stages of spermatogenesis and spatially with the sperm motility apparatus, collectively suggest that this growth arrest-specific gene product may have a role in sperm motility. This postulated role for Gas8 is supported by our observation that highly localized production of Gas8 protein occurs also in the cilia of epithelial cells lining pulmonary bronchi and fallopian tubes and by the flagellar association of a *Trypanosoma brucei* ortholog of Gas8.