Genomic and cytogenetic characterization of the porcine imprinted and three non-imprinted domains orthologous to the human Prader-Willi syndrome chromosome region

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2nd International Hyperphagia & 26th Annual PWSA (USA) Conferences, Pennington Biomedical Research Center, LSU, Baton Rouge, LA, October 17-20, 2012

Abstract

Introduction/Background: Prader-Willi syndrome (PWS) is a multistystem disorder caused by loss of function of a ~2 Mb cluster of ~12 paternally-expressed, imprinted genes in human chromosome 15q11-q13. Cardiornal features include neonatal failure to thrive, abnormal body composition, short stature with GH deficiency, and childhood-onset hyperphagia and obesity, among other endocrine and behavioral abnormalities. Although mouse models of PWS recapitulate some of the clinical components of the disorder, none develop early onset hyperphagia or the severe obesity of the human disease. Therefore, alternative animal models are needed to study the biomedical basis and therapeutic approaches for the eating disorder and obesity. Miniature pigs may provide an ideal model for PWS and other body fat disorders, since they have a more similar body size, physiology, anatomy, and genome to human than does the mouse, and hence may be more susceptible to development of obesity. Furthermore, technologies exist in the pig to produce genetic models of disease.

Results/Discussion: Prior to this study, the pig PWS-orthologous region was poorly represented in the pig genome sequence. Using sequence databases to screen for phylogenetically conserved sequences from the PWS domain, we generated in silico BAC and fosmid contigs spanning most of the pig PWS-homologous imprinted domain. Although mouse models of PWS recapitulate some of the clinical components of the disorder, none develop early onset hyperphagia or the severe obesity of the human disease. Therefore, alternative animal models are needed to study the biomedical basis and therapeutic approaches for the eating disorder and obesity. Miniature pigs may provide an ideal model for PWS and other body fat disorders, since they have a more similar body size, physiology, anatomy, and genome to human than does the mouse, and hence may be more susceptible to development of obesity. Furthermore, technologies exist in the pig to produce genetic models of disease.

Conclusions: This work has identified the genetic structure of imprinted genes, transcriptional and imprinting cis-regulatory elements, and chromosome evolutionary breakpoints in the PWS-orthologous domain in pig. As a consequence, it is now possible to consider the development of pig models of PWS.