TSG101 Conditional Knockout Mouse

**Technology Fields:** Research Tools - Animal Models  
**Technology ID:** 196

**Summary**
The protein encoded by the Tumor Susceptibility Gene 101 (Tsg101) has a variety of important functions including the regulation of cellular proliferation, endosomal sorting of growth factor receptors, and viral budding. Tsg101 was originally identified in a screen for potential tumor suppressors, but this gene may actually be an oncogene since it has been shown to be overexpressed in a subset of breast and ovarian cancers. Deficiency in Tsg101 in various cell lines causes severe growth inhibition and cell death due to the inactivation of cyclin-dependent kinase 2, causing a growth arrest at the G1/S checkpoint. Other recent studies suggest that Tsg101 also plays a central role in the regulation of endosomal sorting, allowing for the recruitment of ESCRT-1, an endosomal sorting complex, to the endosome. Interestingly, because of its importance in the regulation of endosomal sorting, Tsg101 has been shown to be important in the regulation of viral budding. Researchers at The University of Nebraska Medical Center have developed a Tsg101 conditional knockout mouse. The mating of a conditional Tsg101 mouse with an MMTV-Cre strain has resulted in the excision of the first coding exon of the Tsg101 alleles that contains the transcriptional start codon thus creating a Tsg101 null mutation. Due to the variety of cellular functions controlled by Tsg101, this conditional knockout model will be a valuable tool for further understanding the role of Tsg101.

**Market Value**
The Tsg101 conditional mouse model will be useful for further understanding the cellular function of Tsg101. It will also provide a valuable tool for determining the role of Tsg101 in the development of a variety of diseases such as cancer or HIV. Furthermore, this model could prove useful for discovering novel cancer therapeutics and antiretroviral therapies.

**Publications**
Tsg101 Conditional Knockout Mouse Model
The protein encoded by the Tumor Susceptibility Gene 101 (Tsg101) has a variety of important functions including the regulation of cellular proliferation, endosomal sorting of growth factor receptors, and viral budding [1, 2, 3, 7]. Tsg101 was originally identified in a screen for potential tumor suppressors, but this gene may actually be an oncogene since it has been shown to be overexpressed in a subset of breast and ovarian cancers [4, 8]. Deficiency in Tsg101 in various cell lines causes severe growth inhibition and cell death due to the inactivation of cyclin-dependent kinase 2, causing a growth arrest at the G1/S checkpoint [2, 7], demonstrating its importance in cellular growth and proliferation. Through the use of the Tsg101 conditional knockout mouse model it is now well established that Tsg101 is essential for cellular proliferation, survival, and normal development of embryonic and adult tissues [2, 7].

Recent studies suggest that Tsg101 also plays a central role in the regulation of endosomal sorting. Tsg101 interacts with ubiquitinated receptors and the early endosome protein HRS, allowing for the recruitment of ESCRT-1, an endosomal sorting complex, to the endosome [3, 6]. Interestingly, Tsg101 is also important in the regulation of viral budding. Studies have demonstrated that a number of retroviruses, such as HIV, utilize Tsg101-mediated endosomal sorting to facilitate viral budding, making it an intriguing target for antiviral therapies [1, 5].
Development of the Tsg101 conditional knockout mouse

Due to its wide range of functions Tsg101 presents itself as a potential therapeutic target for a number of diseases ranging from cancer to viral infections. To better understand the function of Tsg101 in vivo, Dr. Kay-Uwe Wagner at the University of Nebraska Medical Center (UNMC) developed a Tsg101 conditional knockout mouse model. The conditional knockout allele is floxed: loxP sites surround the first coding exon of Tsg101. The Cre-mediated deletion of the first coding exon results in a true null mutation [7]. This model allows for deletion of Tsg101 in selected tissues providing a way to study Tsg101 function. This mouse model is an excellent tool for studying the function of Tsg101 in vivo, and provides a way to discover novel therapeutics that regulate Tsg101 function.

Licensing Opportunities

Licensing opportunities for the Tsg101 conditional knockout mouse model are now available through UNeMed. The Tsg101 conditional knockout mouse model is an invaluable research tool offering new opportunities to investigate the role of Tsg101 in the development and progression of cancer.
Kay-Uwe Wagner is an Associate Professor at the University of Nebraska Medical Center. His laboratory has extensive expertise in deleting genes in a tissue-specific and temporally controlled fashion using the Cre-loxP recombination system. Their current projects include the analysis of prolactin signaling through the Jak2-Stat5 pathway, the cloning of a new mammary epithelial population from parous females, and studying the role of the Tsg101 gene during cell cycle regulation and neoplastic transformation. For more information on Dr. Wagner's work please visit: http://www.unmc.edu/wagnerlab/index.html
UNeMed is a private, for-profit company that provides technology transfer services to the University of Nebraska Medical Center. UNeMed is dedicated to developing and fostering relationships with industry to transfer UNMC intellectual property from the academic laboratory to the industry. Consistent with its focus, UNeMed continues to seek industrial licensing opportunities to enhance the development of its technologies and foster scientific breakthroughs at UNMC. Researchers at the University of Nebraska Medical Center develop research tools daily as part of their innovative research, which UNeMed works to make available to industry partners.

In addition to the Tsg 101Conditional Knockout Mice, UNeMed currently offers an extensive portfolio of over 100 technologies available for licensing. UNeMed negotiates approximately 300 contracts per year enabling research and collaboration at UNMC. For more exciting technologies please visit www.UNEMED.com.

UNeMed’s Team (from left to right): Michael Dixon, President / Chief Operating Officer, Steve Schreiner, Sr. Licensing Specialist, Joe Runge, Licensing Specialist, Jason Nickla, Licensing Specialist and James Linder, Chief Executive Officer;
References:


