

13 DEVELOPMENT OF A PRECLINICAL CD98HC MOUSE MODEL FOR THERAPEUTIC STUDIES

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Background Angiogenesis is essential for many developmental and pathological processes, is dependent on endothelial cell proliferation and migration, and is partially directed by integrin signaling. CD98HC has been shown to participate in integrin signaling, and most notably, has been implicated in tumor cell growth. Developing preclinical models to study anti-tumor activities by targeting CD98HC is important for downstream translational applications.

Methods To this end, Biocytogen generated a humanized (B-hCD98HC) mouse model. Using gene editing technology, exons encoding the extracellular domain of murine *Cd98* were replaced by the corresponding sequences of human *CD98*. Human *CD98* gene expression was analyzed by RT-PCR in renal tissue isolated from C57BL/6 (+/+) and homozygous B-hCD98HC (H/H) mice. We next analyzed human CD98 protein expression by flow cytometry using splenocytes isolated from C57BL/6 (+/+) and homozygous B-hCD98HC (H/H) mice. Finally, we examined human CD98 protein expression by immunofluorescence using brain tissue isolated from C57BL/6 (+/+) and homozygous B-hCD98HC (H/H) mice and processed into paraffin sections. Paraffin sections were co-stained with an anti-mouse CD31 antibody to visualize microvascular endothelial cells and an anti-human CD98HC antibody.

Results We first confirmed human *CD98* gene expression in renal tissue from B-hCD98HC mice by RT-PCR. Flow cytometric analysis detected human CD98 protein expression in splenocytes from B-hCD98HC mice. Similarly, human CD98 protein expression was observed by immunofluorescence in brain microvascular endothelium from B-hCD98HC mice.

Conclusions We have established a humanized B-hCD98HC mouse model that exhibits robust expression of human CD98HC, which can be used for preclinical studies to assess the efficacy of novel therapeutic agents.

Ethics Approval All animal studies were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of Biocytogen Beijing Co., Ltd.

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