Generation of light-producing somatic-transgenic mice using adeno-associated virus vectors

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Germ line light producing transgenic mice, where luciferase expression is controlled by a surrogate promoter or by a minimal promoter downstream of tandem, synthetic, transcription factor binding elements, are used to provide an *in vivo* readout of disease processes. However, germ line transgenics are expensive to generate and maintain.

Using a standard Gateway® cloning system we previously established a library of more than 25 lentivirus biosensors which we validated in the context of luciferase-expressing lentiviral vectors[1]. Administration of these vectors to neonatal mice permitted monitoring of signalling pathways by whole body bioluminescence imaging.

To achieve even wider transduction we ported this system to the AAV backbone. In this study, we aimed to obtain preliminary validation of this versatile system by delivering NFκB driving a luciferase reporter construct to the nervous system of neonatal mice to generate somatic-transgenic mice using adeno-associated viral (AAV) vectors.

AAV8 serotyped vector was injected intracranially to outbred CD1 neonatal (P1) mice and luciferase expression was monitored continually by whole body bioluminescence imaging of conscious mice.

Intracranial injection of AAV8 NFκB biosensor showed a widespread luciferase expression throughout the brain and along the length of the spinal cord. Interestingly, even when we administered AAV8 NFκB biosensor intravenously at P1, luciferase expression was still strongest in the brain and spine. This is surprising since previous studies have shown that AAV8 serotype transduces most organs after neonatal injection (Inagaki et al. 2008).

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Our observations demonstrate the feasibility of using AAV vectors to generate somatic transgenic light producing transgenic mice. Moreover, they also reveal a surprisingly high degree of NFkB signalling in the nervous system compared with other tissues.

We now aim to systematically test other transcription factor reporters in this model.

1. Buckley SM, Delhove JM, Perocheau DP, Karda R, et al.. Sci Rep. 2015;5(11842)

2. Inagaki K, Piao C, Kotchey NM, Wu X, and Nakai H.. J Virol. 2008;82(19):9513-24.