DEVELOPMENT OF A NOVEL NEAR-INFRARED REPORTER SYSTEM FOR *IN VITRO* AND *IN VIVO* IMAGING OF CANCER

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Key words: *In vivo* optical imaging, near-infrared, reporter gene, acute myeloid leukaemia

In the study of cancer and development of clinically effective therapeutics, evaluation in relevant preclinical murine animal models of human disease is crucial. As are the methodology to observe disease development in the animals. Optical imaging detects cells labelled with an optical reporter system through the excitation and subsequent detection of fluorescence/chemiluminescence. The method allows fast acquisition of mouse whole body images and disease development can non-invasively be followed over time. We have applied this technique in a model of Acute Myeloid Leukaemia (AML), using a novel reporter system.

The properties of the reporter system is of importance for early and accurate detection of leukemic lesions at depths, for instance in blood rich tissues such as the bone marrow. In fluorescent reporter systems that operates at far red to near infrared wavelengths (600-900 nm), absorbance decreases dramatically and allows light to penetrate 1-2 cm of tissue. This is very beneficial for *in vivo* studies compared to conventional visible range reporter systems (400-650 nm) such as green fluorescent protein (GFP), which has a limited *in vivo* use.

Here, we describe the novel use of a combination of a non-mammalian enzymatic (NME) reporter gene and an inducible near-infrared fluorescent dye as a reporter system in human AML cells. The system permis in vitro through to in vivo applications with one reporter. Labelled AML cells are engrafted in NOD/SCID mice and visualized by non-invasive fluorescence lifetime optical imaging. The system enables early detection of leukemic infiltrates, accurate disease staging and detection of deep tissue infiltrates that are not possible with GFP. Preliminary data both *in vitro* and *in vivo* also show that NME^+ AML cells are responsive to antibiotics acivated by NME.