De ondertekende formulieren sturen naar:
Erna Dewil, Proefdierencentrum, Herestraat 49 bus 501, 3000 Leuven.

KATHOLIEKE UNIVERSITEIT LEUVEN

Aanvraag tot aanpassing aan een proefdierexperiment – *application for a modification to an animal experiment*

Laboratorium (*laboratory*): Theragnostic Laboratory

Erkenningsnr laboratorium (*license number*): LA1210224

Laboratoriumdirecteur (*laboratory director*): Yicheng Ni

Projectnummer (*project number*): P147/2013

Titel van het onderzoeksproject (*title of the research project*):

MRI-navigated target selection for diagnosis and treatment of hepatocellular carcinomas

Gelieve aan te geven om welke aanpassing het gaat (*please indicate what the modification is about*)

☐ **Verlenging van het project (maximum 1 jaar, voor verlenging van meer dan 1 jaar dient een volledig dossier te worden ingevuld)** (*change in duration of the project, max 1 year allowed*) Begindatum/*starting date*: Einddatum/*end date*:

☐ **Wijziging in techniek/manipulatie**/*change in technique or manipulation*

☒ **Wijziging in proefdieren – extra dieren nodig – inschatting pijn, lijden en letsel**/ *change in animals – need for extra animals - estimate of pain, suffering and lasting harm*

Aantal *number*	Diersoort *species and strain*	Gemiddelde duur van de proef (dagen, weken, maanden) *Mean duration of the experiment (days, weeks, months)*	Gemiddelde duur van pijn, lijden en letsel (dagen, weken, maanden) *Mean duration of pain, suffering and lasting harm (days, weeks, months)*	Graad van pijn, lijden en letsel (geen, gering, matig, ernstig, ondefinieerbaar) *Estimate of pain, suffering and lasting harm (none, low, moderate, severe, undefinable)*
50	SD or Wistar rats	5 months		Low to moderate

Motivatie voor de gevraagde aanpassing en van het aantal benodigde dieren of **motivatie voor en beschrijving van de aangepaste technieken**/ *justification for the modification and the number of animals and justification for the modified techniques*

In order to compensate the unexpected animal loss during the orthotopical HCC experiment, extra 50 rats would be needed, half of which for methodological validation and the other half for experiments. Specifically, 24 SD rats will be randomized into 4 groups of 6 each after inducing HCCs: Group A receives injections of 2 solvents; Group B receives an injection of Combretastatin A4 phosphate (CA4P) followed by the injection of ^{124}I-Hypericin (^{124}I-Hyp) solvent; Group C receives an injection of CA4P solvent followed by the injection of ^{124}I-Hyp and Group D receives the injections of CA4P and ^{124}I-Hyp.

Datum/*date*: Feb. 23, 2016 Handtekening van de laboratoriumdirecteur/*signature of the laboratory director*:

Advies (voorbehouden aan de Ethische Commissie) (*for the Ethical Committee*):

☐ gunstig/*favorable* ☒ gunstig mits aanpassingen/*provided favorable adjustment* ☐ ongunstig/*rejected*

Inschatting van pijn, lijden of letsel door de Ethische Commissie/*estimate bij the Ethical Comittee*

☐ geen/*none* ☐ gering/*minor* ☒ matig/*moderate* ☒ ernstig/*severe* ☐ ondefinieerbaar/*undefinable* Datum/*date*: 10.05.2016

Commentaar en opmerkingen/*comments and remarks*

10.

De Voorzitter/ *the Chairman*

Erna Dewil

From: Yewei Liu
Sent: vrijdag 8 april 2016 18:49
To: ECD Proefdierencentrum
Subject: Re:

Dear Erna,

Sorry for my delayed reply, because recently I have been busy with our experiment on a batch of ^{124}I-hypericin on the transplanted liver tumor model with CA4P-induced intratumoral necrosis. This study aims at evaluating the necrosis avidity of ^{124}I-hypericin by doing γ-counting, autoradiography and *in vivo* microPET.

According to our previously published research:

1. http://link.springer.com/article/10.1007/s11095-013-1159-4/fulltext.html
2. https://www.researchgate.net/publication/257531806_Targetability_and_Biodistribution_of_Radioiodinated_Hypericin_Comparison_between_Microdosing_and_Carrier-Added_Preparations

The necrosis avidity of the radiotracer is going to be determined, and 6 animals per group could possibly provide statistically significant differences. The power would be 0.9, and the alpha would be 0.05, with the empirical differences of the tumor volumes of 0.4-2.6 cm^3 before and after treatment, and the necrosis ratios of 19-71% between VDA-induced tumor necrosis over entire tumor with the variabilities (SDs) of 0.2-0.7 cm^3 and 11-18%, respectively (see Table III in the above cover-page publication 1). The main difference between our previous experiment and the upcoming experiment is the different tracers used, i.e. ^{123}I-hypericin versus ^{124}I-hypericin. Thus, we expect n=6 would be the minimum group size for our upcoming experiment.

Thanks in advance for your consideration. Should you need any further information, please do not hesitate to contact me.

Best regards,

Yewei

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Yewei Liu, MD, PhD candidate
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From: Erna Dewil on behalf of ECD Proefdierencentrum
Sent: Wednesday, March 16, 2016 1:16 PM
To: Yewei Liu
Subject: RE:

Dear Yewei