MATERIAL TRANSFER AGREEMENT

(for non-commercial use by academic institutions)

Acox2$^{+/-}$ and *Acox2*$^{-/-}$ mice

KATHOLIEKE
UNIVERSITEIT
LEUVEN

This material transfer agreement ("Agreement") is executed between

Katholieke Universiteit Leuven, for the purposes of this Agreement represented by KU Leuven Research & Development, with its offices at Waaistraat 6, box 5105, 3000 Leuven, Belgium, acting on request of Professor P. Van Veldhoven of the Department Cellular and Molecular Medicine (LIPIT), hereinafter referred to as "**Provider**"; and

INSTITUTION NAME, with offices in address, VAT number ..., hereinafter referred to as "**Recipient**";

Provider and Recipient hereafter also individually or jointly referred to as the "Party" or the "Parties".

Whereas, Provider, in particular the research group of Prof. Dr. P. Van Veldhoven (Provider's scientist) has developed and owns certain materials and information and rights relating to said materials and information.

Whereas, Recipient wishes to obtain the material identified as Acox2$^{+/-}$ and Acox2$^{-/-}$ mice for the purpose of its academic internal non-commercial research as specified in Annex A.

THEREFORE IT IS AGREED BY THE PARTIES AS FOLLOWS:

1. Definitions

1.1. "Confidential Information" shall mean the information disclosed by Provider to Recipient related to the Material within the scope and purpose of the Research and which is (i) disclosed in tangible form and marked "Confidential" or "Proprietary" or similarly marked by the Provider before disclosure to the Recipient; or (ii) disclosed in intangible form such as electronically, orally or by visual inspection, identified as confidential at the time of disclosure and summarized in writing by Provider within thirty (30) days of disclosure; or (iii) obviously confidential in nature.

1.2. "Inventions" shall mean any and all inventions, know-how, materials, substances and other results conceived or generated by Recipient (whether patentable or not) and related to the Material or its use, or developed using the Material, including but not limited to Modifications or inventions related to the use of Modifications.

1.3. “Material” refers to the material that is covered by this Agreement and shall mean Original Material, Progeny and Unmodified Derivatives, and any part thereof.

1.4. “Modifications” for the purpose of this Agreement shall mean substances or materials created or developed by the Recipient which contain or incorporate any form of the Material or parts of the Material.

1.5. “Original Material” shall mean all materials provided by Provider, as defined in Annex A attached hereto as well as any medium in which the Original Material is provided, any parts of the Original Material (such as, but not limited to, any reproductive, genetic or other replicable parts). The Original Material is an animal and can be cross-bred. Any cross-bred progeny, descendants of the cross-bred progeny and any part thereof (such as hybrid cell lines) that contains the same mutation(s) as the Original Material, are considered Modifications.

1.6. “Progeny” shall mean all unmodified descendants from the Original Material, such as virus from virus, cell from cell, or organism from organism.

1.7. “Research” shall mean the non-commercial research project and non-commercial research activities as defined in Annex A.

1.8. “Unmodified Derivatives” shall mean any substances created by Recipient which constitute an important unmodified functional sub-unit or product expressed by the Original Material, e.g. sub clones of unmodified cell lines, purified or fractionated sub-sets of the Original Material, proteins expressed by DNA or RNA, monoclonal antibodies secreted by a hybridoma cell line, sub-sets of the Original Material such as novel plasmids or vectors.

2. Use of the Material

2.1. The Material is made available to Recipient as a service to the research community.

2.2. Except as explicitly provided herein, this Agreement does not imply any direct or indirect license. Nothing in this Agreement shall be deemed to grant Recipient any rights under any patent or patent application, nor any direct or indirect rights or license to use, or permit the use of, any products or processes containing, using, or derived from the Material or any Modifications for commercial purposes.

2.3. The Material and any Modifications will be used for academic internal non-commercial research purposes only. Recipient will use the Material and any Modifications solely for the Research (as specified in Annex A) at Recipient facilities under the direction of Recipient’s scientist <name of Recipient's scientist>. The Parties agree that commercial purposes shall include any and all research activities generating revenues for Recipient or any transfer or license of rights to non-academic third parties, including but not limited to sale or license of the Material or Modifications, use of the Material or Modifications in industry sponsored projects, for screening of compound libraries, to produce or manufacture products for general sale or use of the Material or Modifications in fee-for-service activities conducted for the benefit of a third party.

2.4. Recipient shall not transmit by any means whatsoever all or part of the Material, including that included in Modifications, to any third party without the prior and written consent of Provider. Recipient shall refer any request for the Material to Provider. Provider may make Material available to third parties, both profit and non-profit third parties.

2.5. Recipient undertakes to limit access to the Material or Modifications to those of its employees who have a need to know to execute the Research. Recipient undertakes to have any of its personnel involved in the Research comply with the provisions of this Agreement.

2.6. The Recipient agrees to use the Material in compliance with all applicable statutes and regulations, including, for example, those relating to research involving the use of animal subjects or recombinant DNA. This Material is not for use in human subjects.

3. Intellectual Property

3.1. The Material is and remains the property of Provider. Recipient agrees not to apply for any patent or any other proprietary title which would claim the Material or its use. Provider furthermore retains ownership of any form or part of the Material included in Modifications.

3.2. Recipient will promptly and fully disclose in writing to Provider any and all patentable or commercially useful Inventions.

3.3. Ownership of any Inventions will be negotiated and agreed by the Parties in good faith taking into account the Parties' respective contributions to such Inventions. The Provider will in any case be granted a royalty free, non-exclusive license to any Invention for its internal non-commercial research and teaching purposes. Recipient agrees not to apply for any patent or any other industrial property title, which would claim Inventions, without prior written agreement between Provider and Recipient. In any case, if any revenues result from Recipient's use of the Inventions, the Provider will be entitled to a fair and reasonable share of any such revenues.

4. Confidentiality

Confidential Information shall not be distributed, disclosed, or disseminated in any way or form by Recipient, except to its own employees who have a reasonable need to know the Confidential Information for the Research and who shall be bound by confidentiality obligations at least as stringent as the one provided for in this Agreement. Recipient agrees for a period of five (5) years following expiration or termination of this Agreement, to keep confidential all Confidential Information of Provider. The above obligations of confidentiality shall not apply to any information, which the Recipient can prove: (a) is or becomes part of the public domain, through no breach of this Agreement by Recipient; (b) was in Recipient's possession prior to receipt from Provider; (c) is received by Recipient from a third party free to disclose such information; (d) is subsequently independently developed by Recipient, without use of Provider's Confidential Information; or (e) is approved for release by prior written authorization of the Provider. The above obligations of confidentiality shall furthermore not apply to information to the extent such information is required to be disclosed by operation of law or by court or administrative order. The Recipient will furnish prompt and prior written notice of such requirement to the Provider and will cooperate with the Provider in contesting a disclosure.

5. Publications

5.1. Recipient will have the right to publish and disclose the scientific results of the Research subject to the following procedure. In order to balance the publication rights of Recipient with Provider's proprietary interests in its Confidential Information, the Material and Inventions, as the case may be, Recipient will send the proposed publication or disclosure to Provider for review at least thirty (30)

days prior to the scheduled submission for publication or disclosure. Upon request of Provider, Recipient shall delete from its proposal or disclosure any reference to Provider's Confidential Information. Furthermore, Provider may request a delay of the publication or disclosure for a period of three (3) months from the date of receipt of the publication by Provider in order to protect its intellectual property rights.

5.2. Recipient agrees to mention at least one of Provider's scientists as co-author in any publications reporting use of it, unless otherwise agreed upon. If so, the recipient agrees to acknowledge the Provider and the source of the Material in any publications reporting use of it and to cite Provider's scientist's publication (as will be detailed by Provider) in any publications reporting use of the Material.

6. Warranties and limitation of liability

6.1. Recipient understands that the Material is experimental in nature, and may have hazardous properties. The Provider makes no representations and gives no warranties either express or implied in relation to it. For example, no warranties are given about quality or fitness for a particular purpose; or that the use of the Material will not infringe any intellectual property or other rights of third parties.

6.2. Recipient assumes all liability for damages which may arise from its use, storage or disposal of the Material. The Provider will not be liable to Recipient for any loss, claim or demand made by Recipient, or made against Recipient by any other party, due to or arising from the use, storage or disposal of the Material by the Recipient.

6.3. The liability of Provider for any breach of Provider's obligations under this Agreement will in no event extend to any indirect damages or losses, or to any loss of profits, loss of revenue, loss of data, loss of contracts or opportunity (whether direct or indirect), even if Recipient has advised Provider of the possibility of those losses, or even if they were within the Recipient's contemplation.

6.4. Notwithstanding the foregoing, a Party's liability shall not be excluded or limited in the event and to the extent damages are caused by the wilful misconduct of such a Party and any limitations or exclusions of liability under this Agreement shall not apply to the extent such liability cannot be limited or excluded by applicable law.

6.5. Either Party represent that this Agreement does not, and will not conflict with any other right or obligation provided under any other agreement or obligation that either Party has with any third party.

7. Term & Termination

7.1. This Agreement shall commence on the date of last signature below and will (subject to earlier termination pursuant to clause 7.2) continue for a period of three (3) years after the commencement date.

7.2. Provider may terminate this Agreement if Recipient is in material breach of any of the terms of this Agreement and, where the breach is capable of remedy, Recipient has failed to remedy the same within one (1) month of a written notice from Provider specifying the breach and requiring it to be remedied.

7.3. Upon expiration or termination of this Agreement, Recipient will discontinue use of the Material and Confidential Information which shall be returned to Provider

or be destroyed within thirty (30) days. In case of destruction of the Material and Confidential Information, a written confirmation shall be sent to Provider within forty-five (45) days after the termination or expiration of the Agreement. One record copy of documents may be retained to determine compliance under this Agreement. Recipient will also either destroy the Modifications or remain bound by the terms of this Agreement as they apply to Modifications.

7.4. Any provisions of this Agreement which by their nature extend beyond termination shall survive the termination of this Agreement

8. Miscellaneous

8.1. The Material is provided at no cost (except transportation and handling costs, which will be paid by Recipient).

8.2. This Agreement is personal to Recipient and may not be assigned.

8.3. In the case any provision or part thereof of this Agreement is invalid or void, the Parties undertake to agree on a similar but valid provision, the effect of which is as close as possible to that of the invalid provision or part thereof.

8.4. This Agreement embodies the entire agreement between the Parties hereto as to the subject matter hereof and merges all prior discussions and no provision of this Agreement may be changed except by the mutual written consent of the Parties hereto. No amendment, consent or waiver of terms of this Agreement shall bind either Party unless in writing and signed by the authorized signatories of the Parties.

8.5. All disputes between the Parties in connection to this Agreement shall first be discussed in good faith between the Parties in order to try to find an amicable solution. If no solution can be found to settle the dispute within forty-five (45) days after giving notice of the dispute to the other Party, then the Parties will refer the matter to their higher management (executive level: CEO, President, Rector,....) who are at least authorized representatives for the Parties and who will meet and negotiate in good faith in an effort to resolve the dispute within thirty (30) calendar days after the referral. If the matter has not been resolved within such period, each Party is entitled to submit the dispute to the sole competent courts of Belgium.

8.6. This Agreement shall be governed by and construed in accordance with the laws of Belgium, excluding its conflict of law provisions.

Signed for and on behalf of the **Provider**

Annelies Beckers Scientific Contract Officer	Paul Van Dun General Manager
_____ Signature	_____ Signature

Date:

For Approval:

Provider scientist
Prof.Paul P. Van Veldhoven
Laboratory of Lipid Biochemstry and Protein Interactions
O&N1 Herestraat 49 - box 601
3000 Leuven, Belgium

_____
Signature

Date:

Signed for and on behalf of the **Recipient**

Investigator title	authorized officer title
_____ Signature	_____ Signature
Date:	

ANNEX A

A.1 Description of Original Material

Brief description of original material, referring to article (title, magazine, year, volume, pg)

Mice, hetero- or homozygous for a deletion in the *Acox2* gene (either Δ47 or Δ176), resulting in a truncated and inactive ACOX2 (1). ACOX2 (also called trihydrocoprostanoyl-CoA oxidase, branched chain acyl-CoA oxidase), discovered (2-4) and cloned (5,6) in Leuven, is required for the degradation of pristanic acid and the formation of mature bile acids (1,7).

1. Van Veldhoven P.P., unpublished data.
2. Schepers L., Van Veldhoven P.P., Casteels M., Eyssen H.J. and Mannaerts G.P. Presence of three acyl-CoA oxidases in rat liver peroxisomes. An inducible fatty acyl-CoA oxidase, a non-inducible fatty acyl-CoA oxidase and a non-inducible trihydroxycoprostanoyl-CoA oxidase. J. Biol. Chem. (1990) 265, 5242-5246.
3. Casteels M., Schepers L., Van Veldhoven P.P., Eyssen H.J. and Mannaerts G.P. Separate peroxisomal oxidases for fatty acyl-CoAs and trihydroxycoprostanoyl-CoA in human liver. J. Lipid Res. (1990) 31, 1865-1872.
4. Vanhove G.F., Van Veldhoven P.P., Fransen M., Denis S., Eyssen H.J., Wanders R.J.A. and Mannaerts G.P. The CoA esters of 2-methyl-branched chain fatty acids and of the bile acid intermediates di- and trihydroxycoprostanic acids are oxidized by one single peroxisomal branched chain acyl-CoA oxidase in human liver and kidney. J. Biol. Chem. (1993) 268, 10335-10344.
5. Baumgart E., Vanhooren J.C.T., Fransen M., Van Leuven F., Fahimi, H.D., Van Veldhoven P.P and Mannaerts G.P. Molecular cloning and further characterization of rat peroxisomal trihydroxycoprostanoyl-CoA oxidase. Biochem. J. (1996) 320, 115 121.
6. Baumgart E., Vanhooren J.C.T., Fransen M., Marynen P., Pyupe M., Vandekerckhove J., Leunissen J.A.M., Fahimi H.D., Mannaerts G.P. and Van Veldhoven P.P. Molecular characterization of the human peroxisomal branched chain acyl-CoA oxidase. cDNA cloning, chromosomal assignment, tissue distribution and evidence for the absence of the protein in Zellweger syndrome. Proc. Natl. Acad. Sci. USA (1996) 93, 13748 13753.
7. Van Veldhoven P.P., Vanhove G., Asselberghs S., Eyssen H.J. and Mannaerts G.P. Substrate specificities of rat liver peroxisomal acyl-CoA oxidases: Palmitoyl-CoA oxidase (inducible acyl-CoA oxidase), pristanoyl-CoA oxidase (non-inducible acyl-CoA oxidase) and trihydroxycoprostanoyl-CoA oxidase. J. Biol. Chem. (1992) 267, 20065 20074. 37.

A.2. Description of Recipient's Research using the Material

Brief description of research activities