Delibera n. **326/2017** del Consiglio di Amministrazione del **22/12/2017**

OGGETTO: **Accordo per il trasferimento di materiale tra il Dipartimento di Scienze Biomolecolari (DISB) dell'Ateneo, la ditta XenTech SAS (Francia), il Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES) dell'Università di Bologna**		
N. O.d.g.: 6.6	Rep. n. 326/2017	UOR: Ufficio Ricerca

Nominativo	**F**	**C**	**A**	**As**
Vilberto Stocchi	X			
Giovanni Battista Berloni	X			
Francesca Capodagli				X
Mauro Papalini	X			
Angela Giallongo	X			
Stefano Papa	X			
Luciano Stefanini	X			
Luciana Vallorani	X			
Michele Buffalini	X			
Gianmario Xhemal Doka	X			
Enzo Laveglia				X

Legenda: (F - Favorevole) - (C - Contrario) - (A - Astenuto) - (As - Assente)

Partecipano il Pro-Rettore Vicario Prof. Giorgio Calcagnini e il Direttore Generale Dott. Alessandro Perfetto.

Collegio dei Revisori dei conti			
Nome	**Pres.**	**Ass.g.**	**Ass.**
Dott.ssa Maria Luisa De Carli, Presidente		X	
Dott.ssa Gerardina Maiorano		X	
Dott. Vincenzo Galasso	X		

Il Consiglio di Amministrazione

visto lo Statuto della Università degli Studi di Urbino Carlo Bo, emanato con D.R. n.138/2012 del 2 aprile 2012 e pubblicato nella Gazzetta Ufficiale della Repubblica Italiana, Serie Generale, n. 89 del 16 aprile 2012;

visto il Regolamento di Ateneo per l'Amministrazione, la Finanza e la Contabilità dell'Università degli Studi di Urbino Carlo Bo emanato con Decreto Rettorale n. 276/2013 del 26 giugno 2013;

visto il Regolamento di Ateneo per l'attività in conto terzi, emanato con Decreto Rettorale n. 259/2015 dell'8 giugno 2015 e modificato con Decreto Rettorale n. 540/2016 del 29 novembre 2016, in vigore dal 30 novembre 2016;

visto la Legge 9 maggio 1989 n. 168, e successive modificazioni, recante "Istituzione del Ministero dell'università e della ricerca scientifica e tecnologica";

visto il Decreto Legge 16 maggio 2008 n. 85, convertito, con modificazioni, dalla Legge 4 luglio 2008 n. 121 recante "Disposizioni urgenti per l'adeguamento delle strutture di Governo in applicazione dell'articolo 1, commi 376 e 377, della legge 24 dicembre 2007, n. 244" ed in particolare l'art. 1 con il quale è stato istituito il Ministero dell'Istruzione, dell'Università e della Ricerca;

vista la delibera n. 307/2016 del Consiglio di Amministrazione del 16/12/2016, con la quale sono state approvate le "*Linee guida in tema di valorizzazione dei prodotti della ricerca e di gestione della proprietà intellettuale delle invenzioni*";

vista la delibera n. 183/2017/DISB del Consiglio di Scienze Biomolecolari (DISB) dell'8 novembre 2017, con la quale il Consiglio ha approvato la richiesta del Dott. Michele Guescini di stipula di un accordo per il trasferimento di materiale tra il Dipartimento di Scienze Biomolecolari (DISB) dell'Ateneo, la ditta XenTech SAS (Francia), il Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES) dell'Università Alma Mater Studiorum di Bologna";

considerato che l'obiettivo dell'accordo è quello di verificare se i geni e i miRNA di interesse possano essere quantificati e usati come marcatori circolanti in modelli PDX sensibili alla terapia genotossica. Questa ricerca non sarà limitata alla sola valutazione dei marcatori selezionati in quanto l'approccio usato permetterà di effettuare un'analisi estesa dei miRNA circolanti e degli RNA trasportati da microvescicole/esosomi e, eventualmente, individuare anche nuovi marcatori;

ritenuto che le attività oggetto dell'accordo siano espletabili nell'ambito dell'attività di ricerca alla quale lo stesso Dipartimento di Scienze Biomolecolari (DISB) è istituzionalmente preposto;

ritenuto che l'accordo sia meritevole di accoglimento per le finalità che intende perseguire;

considerato che l'accordo per il trasferimento di materiale assumerà una forma non conforme allo schema tipo di contratto per il trasferimento di materiale inserito nelle *Linee guida in tema di valorizzazione dei prodotti della ricerca e di gestione della proprietà intellettuale delle invenzioni* dall'Ateneo;

sentito il Direttore Generale;

D E L I B E R A

1. di approvare l'accordo per il trasferimento di materiale tra il Dipartimento di Scienze Biomolecolari (DISB) dell'Ateneo, la ditta XenTech SAS (Francia), il Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES) dell'Università Alma Mater Studiorum di Bologna", nel testo sotto riportato;
2. di nominare quale *Principal Investigator* il Dott. Michele Guescini, ricercatore a tempo determinato nel SSD BIO/10 – Biochimica, in servizio presso il Dipartimento di Scienze Biomolecolari (DISB);
3. di delegare il Direttore del Dipartimento di Scienze Biomolecolari (DISB), Prof. Orazio Cantoni, a sottoscrivere l'accordo per il trasferimento di materiale tra il Dipartimento di Scienze Biomolecolari (DISB) dell'Ateneo, la ditta XenTech SAS (Francia), il Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES) dell'Università Alma Mater Studiorum di Bologna".

MATERIAL TRANSFER AGREEMENT

This MATERIAL TRANSFER AGREEMENT ("Agreement") is made by and between

1. XenTech SAS (hereinafter referred as the "Xentech"), a French private company having an address at 4 rue Pierre Fontaine, 91000 Evry, France; and

2. Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES), an Italian not-for-profit research institution, having an address at Via Massarenti, 9 Bologna (UNIBO); and

3. Dipartimento di Scienze Biomolecolari, Università degli Studi di Urbino Carlo Bo, an Italian not-for-profit research institution, having an address at Via Aurelio Saffi, 2, 61029 Urbino, Italy (UNIURB).

UNIBO, Xentech and UNIUR each being referred to as a Party in the present agreement.

WHEREAS

A. Xentech is in possession of breast cancer PDX. All products derived from these models are referred to herein as "Materials" and described more fully in the Annex 1

B. UNIBO has acknowledge expertise in the field of circulating microRNA; and

C. UNIURB has acknowledge expertise in the field of circulating microvesicles and exosomes

D. Xentech is willing to share its Material with the others (the releasing Party hereinafter referred to as the "Provider" and the receiving Party hereinafter referred to as the "Recipient") for the experiments described in Annex 1, subject to the acceptance of the following terms and conditions:

1. The Material furnished to a Recipient pursuant to this Agreement and derivatives thereof (including but not limited to recombination constructs, cultures, subcultures, mutations or other products derived directly from the Material, and any modifications of the Material that contain or incorporate the Material, referred to herein as the "Derivatives") will be maintained within the sole possession and control of said Recipient and its staff and will be used solely and exclusively to conduct the non-commercial Research described in the Annex 1 (hereinafter referred to as the "Research").

2. The Material and any Derivatives will only be used for the Research described in Annex 1.

3. The Material will not be distributed, transferred or sold by the Recipient and/or the Recipient's Investigator, his/her staff to any third party for any purposes whatsoever without the prior written agreement of the Provider.

   The Material and/or any anonymized clinical or experimental data relating to the Materials (the "Information") are being provided to and accepted by the Recipient WITHOUT ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE OR ANY OTHER WARRANTY EXPRESSED OR IMPLIED. The Provider and its directors, officers, employees or agents assume no liability and make no representations in connection with the Material or the Derivatives or the Information or their use by the Recipient.

4. To the extent authorized by laws, the Recipient hereby agrees to defend, indemnify and hold harmless to the Provider and its directors, officers, employees and agents from and against any liability or claim arising from any use of the Material or the Derivatives by the Recipient except where such liabilities or claims arise from the woeful negligence or intentional misconduct of the Provider. Without limiting the foregoing, the Provider makes no representations as to testing of the Material for the presence or absence of any pathogens, and the Recipient assume all risk of harm with respect to such pathogens.

5. Any Information provided to the Recipient by the Provider relating to the Material that is not already in the public domain shall at all times be treated in strict confidence by the Recipient and shall only be disclosed to those persons under the direct supervision of the Recipient's Investigator who need to know such Information for the purpose of conducting the Research, provided always that those persons are informed of the confidential nature of that Information. The Recipient shall not have any obligation of confidentiality with respect to Information that: (a) is or becomes in the public domain through no fault of the Recipient; or (b) is already in possession of the Recipient prior to receipt from the Provider; or (c) is demonstrably developed independently by the Recipient; or (d) is obtained from a third party who is not under a confidentiality obligation to the Provider; or (e) is required by law to be disclosed to a competent judicial or administrative body.

   In the event that Information is required to be disclosed pursuant to subsection e) and to the extent authorized by the law, the Recipient shall notify the Provider to allow the Provider to assert whatever exclusions or exemptions may be available to it under such law or regulation.

6. Title to the Material and/or to any Derivatives and patent rights and other proprietary rights therein are retained by the Provider. No right or license is granted with respect to the Material, any Derivatives, or the Information, except as express set forth herein. Title to all know-how, invention, improvement or discovery whether or not patentable, relating to Material or use thereof which are solely conceived or made by the Provider and any patent applications, and copyrights relating to such know-how, invention, improvement or discovery whether or not patentable shall be solely owned by the Provider.

7. The Recipient shall have the right, consistent with the academic standards, to publish or present the results of the research work performed in accordance with this Agreement. Authorship shall be determined by individual contribution to the Research. Each party agrees not to disclose or publish any Research data or results without first notifying the other party and allowing them sixty (60) days for review and comment.

8. Recipient will keep Provider's Investigator fully informed in confidence of any inventions or discoveries, whether or not patentable that are conceived or reduced to practice by Recipient's Investigator under the Research ("Invention") through a written final report

summarizing the results of the Research within thirty (30) days of completion or termination of the Research thereof. The Recipient and the Provider shall maintain such data in confidence except as specifically provided to the contrary herein. The parties hereto shall have the right to use such data for research and educational purposes only.

9. Such Inventions and any patents derived therefrom shall be owned by the Parties in equal undivided shares.

12. This Agreement shall be effective as of the date of last signature by the Parties ("Effective Date") and shall terminate one (1) year afterwards or on the earlier of the following: (a) Anticipated date for completion of Research; or (b) upon thirty (30) days written notice of termination by either party to the other party, which notice of termination may be provided with or without cause.

13. Notwithstanding the foregoing, those provisions, which by their nature should survive such termination, shall survive such termination, provided however, that no obligations under this Agreement shall survive beyond ten (10) years following the Effective Date.

14. Upon completion of the Research or in the event that Recipient decides not to continue with the Research or in case of early termination of this agreement, any Material, Information and any Derivatives not used in the Research will be either destroyed by the Recipient or, at the request of the Provider, returned to the Provider at the expense of the Provider.

15. Notwithstanding that the Material, Information and/or Derivatives are returned or destroyed pursuant to the paragraph 13, the obligations of secrecy under paragraph 5 shall continue in full force and effect.

16. In the event of a dispute arising between the parties concerning the interpretation or execution of this Agreement, the parties shall attempt to resolve the issue amicably. If a mutually satisfactory resolution cannot be found, such dispute shall be submitted to the jurisdiction of the laws and courts where the defendant is legally incorporated.

Execution Version

Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES)

Agreed and accepted

By :

Head of Department
Prof. Mauro Gargiulo

Date :

XenTech

Agreed and accepted

By:

President
Jean-Gabriel Judde

Date :

Dipartimento di Scienze Biomolecolari (DiSB) UNIURB

Agreed and accepted

By : Head of Department
Prof. Orazio Cantoni

Date : _____

DIMES's Investigator

Signature:

Dr.ssa Manuela Ferracin, PhD

Xentech's Investigator

Signature:

Name: Stefano Cairo

DiSB's Investigator

Dr. Michele Guescini, PhD

Annex 1

VHIO Research Plan
Xentech Research Materials: All material derived from breast cancer PDXs included in the following list:

PDX ID
HBCx-1
HBCx-2
HBCx-6
HBCx-7
HBCx-8
HBCx-9
HBCx-10
HBCx-11
HBCx-12B
HBCx-14
HBCx-15
HBCx-16
HBCx-17
HBCx-23
HBCx-24
HBCx-27
HBCx-28
HBCx-30
HBCx-31
HBCx-33
HBCx-39
T168
T174
T180R
T298
T311R
T330
T381

Research Project:
-Validation of a gene and microRNA expression signature as early indicator of tumor genomic stress and sensitivity to genotoxic treatment in the blood of PDXs.

-identification of new circulating biomarkers as early indicators of tumor genomic stress and sensitivity to genotoxic treatment

Background: Previous studies on the effects of genotoxic chemotherapy in a series of breast cancer PDXs showed that treatment with cyclophosphamide or the combination of adriamycine and cyclophosphamide (AC) induced the shared overexpression of a collection of

genes, including several interferon-regulated genes, in tumors that were responsive to chemotherapy. From this collection, a list of 21 genes and miRNAs with the most significant p value was selected and includent in a patent application. The overexpression these markers in tumor cells following genotoxic treatment is associated with DNA damage and repair, activation of the DNA-damage checkpoints. Overexpression of these markers is transient, with a peak of expression in treated tumor between 7 and 14 days post-treatment, and reverts to normal levels upon tumor regrowth. We hypothesize that the observation done in the tumor tissue can be transposed to the blood, particularly as it is known that tumor cells release miRNAs and micro-vescicles/exosomes by default or in response to treatment.

The goal of this project is to evaluate if the genes and microRNAs of interest can be retrieved as circulating markers in PDX sensitive to genotoxic treatment. This investigation will not be limited to the validation of the selected markers but the methodological approach will allow to gain a comprehensive analysis of circulating microRNA and micro-vescicle /exosome RNAs, to possibly identify new markers.

Exosome isolation will be run at UNIURB, whereas RNA extraction and circulating microRNA analysis will be performed at UNIBO