Vertex Pharmaceuticals/Oregon Health & Sciences University Research Agreement

REQUEST FOR PROPOSALS 2010-2011

There are two funding opportunities available under the Vertex Pharmaceuticals/Oregon Health & Science University Research Agreement for collaborative and translational research projects:

1. Translational Research Proposals
2. Sponsored Research Proposals

Note: Cross-disciplinary collaborations may be considered more favorably, based on the potential for synergy, with full-level funding of each collaborating group (labs, clinics etc.)

Translational Research Proposals

Pre-proposals are due June 10, 2010 / Full proposals (invitation only) due July 13, 2010

OHSU and Vertex are soliciting proposals for collaborating in translational research. The focus of these projects are to target underlying mechanisms of disease at a sub-organism level and studies to gain a mechanistic understanding of disease (e.g. imaging studies.). This includes:

- studies on cells/tissues from humans to understand mechanism of disease
- assay development based on biomarkers for diagnostics and personalized medicine
- development of predictive preclinical models that bridge the gap between basic and human research

The emphasis is to develop research teams that bring together faculty with a broad range of expertise including clinical and basic research. Multi-disciplinary collaborations will be given greater consideration. Translational projects are intended to be collaborative with the potential for research components to be performed at both OHSU and Vertex.

Translational Research Proposals will be considered from the following areas:

Hepatocellular carcinoma (HCC) and liver disease:
1. Non-biased identification and characterization of putative liver cancer stem cells
   a. Identification and characterization of tumorigenic stem cells from stage II/III hepatocellular carcinoma (HCC) of cirrhotic/alcoholic/obese etiology.
   b. Comparison of HCC-derived tumorigenic cells of differing etiology (cirrhotic/alcoholic/obese vs. hepatitis C infected vs. hepatitis B infected)
      i. Isolation/identification of stem cells by functional/operational methods unbiased by the use of presumed markers of stem cells
2. Identification and/or validation of HCC disease biomarkers for use in preclinical model characterization and clinical disease progression.

Animal Models and Non-Invasive Imaging for Multiple Sclerosis:
   a. Models in rodents and non-human primates and/or those mimicking progressive MS disease for the potential future testing of new drug candidates.
   b. Multimodal imaging approaches capable of detecting longitudinal changes in patients and techniques applicable to preclinical models, including new or improved methods to:
      i. Image myelin, myelin loss and repair in both white and gray matter areas of the brain.
      ii. Reduce elapsed time to see significant changes in patients.
      iii. Develop new or improved methods of MRI or PET imaging in the CNS.
2. Development of imaging techniques capable of detecting global and regional reductions in brain volume.
3. Identification and/or validation of MS and remyelination biomarkers for future use in preclinical model characterization and clinical disease progression.

**Inflammatory Bowel Disease (IBD):**
1. Identify pathways associated with steroid resistance or steroid-dependence of IBD patients having undergone induction therapy.
   b. Identify candidate genes or biomarkers associated with susceptibility to Crohn’s Disease (CD) and/or Ulcerative Colitis (UC), potentially exposing new therapeutic strategies for steroid resistant IBD.

**To apply:** OHSU faculty may submit proposals. Postdoctoral fellows and graduate students are not eligible. If you are interested in submitting a proposal, please contact the Technology Transfer and Business Development Office with a brief (two-page), non-confidential pre-proposal. These pre-proposals will be provided to Vertex so that scientists from both organizations may participate in developing a detailed proposal based on mutual agreement. Pre-proposals should be submitted electronically to Arvin Paranjpe, JD, Technology Coordinator, paranjpe@ohsu.edu. Pre-proposals are due June 10, 2010. Please include VERTEX RFA in the subject line.

**Amount:** The funding for these projects is expected to be at $150,000 per year, which will include a 25% indirect rate, translating in to $120,000 in direct costs and $30,000 in indirect costs) and will also include matching funds from OCTRI and the OHSU Hospital for a total of $200,000 per project plus up to an additional $25,000 in in-kind services from OCTRI in Research Services.

**Sponsored Research Proposals**

*Proposals due July 13, 2010*

OHSU and Vertex Pharmaceuticals welcome new submissions as well as proposals that extend the findings of currently funded work through previous Vertex/OHSU proposals. Specifically, proposals should address one of the following areas:

**Molecular and Cell Biology of Neurodegeneration and Neuroregeneration:**
Regenerative medicine is likely to shape therapies of the future, particularly for neurodegenerative diseases. Vertex is seeking new proposals for studies that will investigate a number of different aspects of neurodegenerative disease and neuroregenerative processes and develop tools for drug discovery in the following areas:

1. Exploration of the basic biology of neurodegenerative processes (axonal degeneration and demyelination) and neuroregeneration (CNS stem cell recruitment and differentiation to generate functional systems), including the use of new animal models.

2. Elucidation of transcriptional and epigenetic pathways regulating neurogenesis and identification of new therapeutic targets, utilizing the following methodologies.
   a. MicroRNAs controlling neurogenesis
   b. Transcriptional regulators of neurogenesis
   c. Epigenetic networks to reprogram pluripotency (iPS cell induction)

3. Investigation of the disruption of mitochondrial dynamics and cell metabolism in neurodegenerative diseases including, but not restricted to Huntington’s chorea and multiple sclerosis.
   a. Role of mitochondria and metabolic status in axonal degeneration

4. Identification and/or validation of clinical and/or translational biomarkers for neurodegeneration and neuroregeneration.

Confidential 22 April 2010
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**Amount:** Up to $75,000 is available for one year projects (including the indirect rate of 25% - for example a total budget of $75,000 would cover direct costs of $60,000 and indirect costs of $15,000 at a reduced rate of 25%).

**Review**

The Translational Research Proposals and the Sponsored Research Proposals will be evaluated jointly by an OHSU review panel consisting of faculty from the relevant areas of interest and by a Vertex-constituted panel.

The selected applications for the Sponsored Research Proposal ($75,000) will be awarded based on this review.

The selected pre-proposals for Translational Research Projects will require joint proposal development by OHSU and Vertex scientists.

**Timelines**

1. Non-confidential pre-proposals for Translational Research Proposals due by June 10, 2010
2. Review of pre-proposals for Translational Research Proposals: June 14, 2010 to June 28, 2010
3. All proposals due by July 13, 2010
4. Selection Committee meeting: July 21-23, 2010
5. Review and refine proposals: July 13, 2010 to Aug 3, 2010
6. Project start date: Sept 1, 2010