

**Tour de Cure’s mission is   
to cure cancer**

**Expression of Interest**

**ELIGIBLE For ABN - Item 1 charities under the Deductible Gift recipient status ONLY**

**Financial Year Ending 2015**

**Research Project Funding**

**Closing Date – 22 September 2014**

**For any enquiries or to email applications please contact**

**Jim Hollier**

**02 8073 4000**

**0412 256 542 or** [**jim@tourdecure.com.au**](mailto:jim@tourdecure.com.au)

# Expression Of Interest Application Form details

This is an Expression of Interest (EOI) application form for a Tour de Cure Research Project donation for funds raised in the Financial Year ending 30 June 2015. These applications can only be made by eligible charities that have been categorised under their ABN Deductible Gift Status as an Item 1 Charity and are subject to one year of funding only unless otherwise stated.

## This aPPLICATION IS FOR RESEARCH FUNDING.

***Note: If applying for funding for more than one research project you must submit a separate application for each research project.***

**Research Projects** – these are focused on finding cancer breakthroughs

All research projects will be required to have an annual review completed by the researcher who has received the funding. Funding can be sought for any one of the following:

* 1. Established Research Grant - $200,000
  2. Scott Canner Research Grant - $125,000
  3. TDC’s Surgical Grant with Foundation for Surgery - $100,000
  4. Collaborative Cancer Research Grant -$50,000
  5. Pioneering Cancer Research Grant - $80,000

***Further information and examples of previous funding can be found on our website using the following link*** <http://www.tourdecure.com.au/pages/about-us/cancer-research-rsp/>

## Application Timeframes

**14 August 2014** Expressions of interest **applications open** available on our Website [***www.tourdecure.com.au***](http://www.tourdecure.com.au)or by emailing [info@tourdecure.com.au](mailto:info@tourdecure.com.au).

**22 September 2014** Expressions of interest **applications close** and must be submitted by email prior to this date to [jim@tourdecure.com.au](mailto:jim@tourdecure.com.au)

## Notification of success and funding

**18 December 2014** Notification of successful applications and confirmed funding for research projects.

**18 December 2015** Funds distributed to successful applicants *(****excluding Research Projects under category C****)*

## Terms and conditions for successful applications

Before applying please note the following terms and conditions. In accepting funding from Tour de Cure you agree to provide the following for the term of the funding:

**For all project types** –

* 6-monthly updates (after funding) emailed to Tour de Cure summarising the status of your project including at least two photos (jpg format)
* Promote our partnership including with the media.

**Research projects**  –

1. Provide via email an annual review of research developments and updates, to be completed by the researcher by the end of November in the year the funding is used.
2. Provide via email an update on any breakthroughs with the following information;   
   ***(Definition: The work of researchers that we have funded is recognized by peers either via a published study or an article in the world leading journals of their respective fields.)***
   * Name of organisation
   * Name of researcher
   * Name of paper or article
   * A brief description of the outcome in non-technical terms for website (30-50 words)
   * Date of paper/article published
   * Name of medical journal
   * Year or years that Tour de Cure has funded this project
   * Copy of or link to the article

# Application Form

## How to use this form

**Selection boxes-** You are able to click in the selection boxes (☐) and can deselect these by clicking on them.

To fill in this form you need to complete the relevant sections. All must be completed to be a valid application.

## Organisation application details

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Charity Name | UNSW Australia | | | | |
| Charity ABN No. | 57 195 873 179  ***Note: Must provide a copy of your ABN showing Item 1 under the Deductible Gift Recipient Status*** | | | | |
| Contact Name | Mr Daniel Owens | | | | |
| Position | Director, Grant Management Office | | | | |
| Email | d.owens@unsw.edu.au | | | | |
| Address | Level 3, Rupert Myers Building South Wing (M15) | | | | |
| City | UNSW Sydney | State | NSW | Postcode | 2052 |
| Phone | (02) 9385 7254 | | | | |
| Mobile | N/A | | | | |

***Note: If applying for funding for more than one research project please submit a separate EOI application form for each. Please select only one of the following options.***

***Note that all applications will be reviewed by panels including independent medical specialists.***

### Research Project

##### Established Research Grant ($200,000) Criteria for this grant:

* + Focused on finding a cancer cure for men, women and/or children
  + Applicants must have established research for more than 3 years with published results indicating significant results to help find a cure for cancer
  + Applicants collaborating with results and achieving results across the industry and diseases will be viewed favourably
  + Application to indicate split of researcher, analyst and capital expenditure
  + Key items reviewed are track record, project quality, significance, innovation, translatability & whether funding would make a difference.

##### Scott Canner Young Research Grant ($125,000) Criteria for this grant:

* Focused on finding a cancer cure for men, women and/or children
* Applicants must be up to 3 years post PHD or MBBS at the close of applications
* Applicants collaborating with results and achieving results across the industry and diseases will be viewed favourably.

##### Tour de cure Cancer research scholarship (in collaboration with foundation for surgery) ($100,000) Link: <http://www.surgeons.org/member-services/scholarships-awards-lectures-prizes/research-and-travel-scholarships/#RESEARCHTITLE>

##### Criteria for this grant:

* Selected via Tour de Cure beneficiary partnership with Foundation for Surgery
* Focused on surgical advancements that help find a cure for cancer

***Note applications for this grant are submitted and reviewed via Foundation for Surgery.***

##### Collaborative Cancer Research Grant ($50,000) *Criteria for this grant:*

* Focused on finding a cancer cure for a men, women and/or children
* Funding that is used by multiple researchers across many institutes focused on finding a cancer cure for men, women and/or children

##### Pioneering Cancer Research Grant ($80,000) *Criteria for this grant:*

* Focused on finding a cancer cure for men, women and/or children
* Conducting new research methodology or ground-breaking research not yet published
* Applicants leveraging or collaborating with results and to achieve results across the industry and diseases will be viewed favourably.

### Please nominate which research project you are applying for

### ☒ Established Research Grant ($200,000)

### ☐ Scott canner young Research Grant ($125,000)

### ☐ Collaborative Cancer Research Grant ($50,000)

### ☐ Tour de cure Cancer research scholarship (in collaboration with foundation for surgery) ($100,000)

### Please go to the folowing link to apply for this scholarship: <http://www.surgeons.org/member-services/scholarships-awards-lectures-prizes/research-and-travel-scholarships/#RESEARCHTITLE>

### ☐ pioneering Research Grant ($80,000)

### Research Project - compulsory questions

All research proposals will be reviewed by our Research Advisory Committee other than the following:

Established Research Grant (reviewed by Translational Research Institute panel);

Tour de Cure Cancer Research Scholarship (submitted to and reviewed by Foundation for Surgery).

The Research Advisory Committee includes independent experts to assist Tour de Cure’s board in the evaluation of research projects that fit within our mission and values, and that aim to cure cancer.

As part of the funding agreement, recipients of each grant are required to provide Tour de Cure with an annual review of works to be submitted by the researcher.

**Responses in boxes below to be in font size 12**

|  |  |
| --- | --- |
| **Describe how your organisation works towards finding a cure for cancer (in lay terms)**  Maximum of 150 words | |
| The Lowy Cancer Research Centre’s (LCRC’s) focus is to use its strength, which is the coexistence of childhood and adult cancer researchers as well as basic scientists and clinicians in the one building, to investigate the common pathways to childhood and adult cancer and to rapidly and efficiently translate this research to the clinic.  Our group investigates the ALT cancer cell immortality mechanism, which is relied upon for the continued growth and survival of many of the pediatric and adult cancers for which the current treatments are least successful. We are in the process of developing the first ALT-targeted cancer therapies and diagnostics, based on our discovery and development of the only biomarker and quantitative assay for the ALT cancer mechanism. The LCRC provides all the key infrastructure and expertise - from drug discovery to clinical trial and access to patient specimens, required for our work. | |
| **Full Project Title** | |
| New cures for cancer, using novel technology for ALT-targeted drug discovery. | |
| **Brief description of the project (in Lay Terms)**  Please provide a basic summary to explain the project and the intended result (maximum of 50 words) | |
| We have invented technology that makes it possible to generate the first cancer cures that target the cancer-specific ALT mechanism. We will use our technology for high-throughput screening of the potential cure “universe”, which is the most prospective strategy for discovering ALT-targeted (low side-effect) cancer cures. | |
| Researchers Details  Provide details of researchers (maximum 1 page summary) plus attach separately to this submission a CV of the principal researcher. | |
| **Principle Researcher: Dr Jeremy Henson (please see CV attached)**  I have led a research group for the last four years, am a Senior Lecturer at the University of NSW and have worked as a clinician for 15 years. With 13 years research experience in the ALT cancer immortality mechanism (the alternative telomere-lengthening mechanism to telomerase), I have made significant contributions to my field. Most notably, I predicted the presence of a completely novel type of biomarker and devised an assay to detect it. The assay has the potential to become a clinically useful diagnostic tool and a research tool for the discovery of novel ALT-targeted therapeutics. It is being used by many telomere research groups and has been patented and licensed to Capital Biosciences Inc. My work was recognized by publication in Nature Biotechnology (current impact factor 32.44) and was a significant breakthrough for research into the ALT cancer mechanism, which was in need of both a quantitative assay and an ALT-specific molecule in order to progress. My background in biophysics, molecular oncology and the clinical contexts in which my biomarker and assay could be used, is proving useful for their translation into cancer diagnostics and therapeutics. My contribution to ALT research demonstrates good quality, with my average citations per first author publication 2.5x the average for the ALT topic, and includes a review that is still the most cited review on the ALT mechanism. I was also involved in the work that pioneered the study of ALT in different types of cancer and I developed the techniques that facilitated this. Over the last three years I have contributed to grant review, student review, recruitment and biobanking committees, as well as supervision and thesis examination for PhD students, and tuition of Bachelor students. | |
| **Associate Investigator: Dr Greg Arndt, Manager, ACRF Drug Discovery Centre for Childhood Cancer**  Dr Greg Arndt established the ACRF Drug Discovery Centre for Childhood Cancer at Children’s Cancer Institute based in the Lowy Cancer Research Centre. This Centre houses a state-of-the-art high-throughput small molecule screening facility to assist in drug discovery and development. Dr Arndt received his PhD from the University of Saskatchewan in Canada in 1993 and worked as a post-doctoral fellow at the R.W. Johnson Pharmaceutical Research Institute. Prior to joining Children’s Cancer Institute, Dr Arndt was Research Director and Project Leader with Johnson & Johnson Pty Ltd, where he spent 15 years in increasingly senior roles focusing on developing novel therapeutics. In addition to industry experience, Dr Arndt has also had significant academic involvement being an Adjunct Senior Lecturer and Senior Visiting Fellow at the University of New South Wales. He has successfully trained several Honours and PhD students, published numerous manuscripts in high quality journals and contributed to several international patent applications. | |
| **Collaborating Investigators: OncoSENS Laboratory, SENS Research Foundation, California, USA**  The OncoSENS Lab was founded by David Halvorsen in 2012, with the aim of developing the research tools for discovering ALT-targeted cancer therapies. Dr Haroldo Silva joined and has been leading the OncoSENS Lab since 2013. They have made remarkable breakthroughs in a very short time in the ALT field. They are the only lab to have advanced the APB Assay (for ALT cancer activity) into (i) a quantitative assay and (ii) a high-throughput assay, both of which are significant developments. The OncoSENS Lab has also advanced the C-Circle Assay for ALT into an ELISA based assay, which required an inventive step and is subject to a provisional patent. As part of a successful collaboration with Dr Henson’s Lab, they have also advanced the C-Circle Assay into a homogenous assay suitable for automation and high-throughput screening, which is subject to a provisional patent (in preparation). These works of the OncoSENS lab are being prepared for publication and was presented at the 2014 EMBO conference on Telomeres, Telomerase and Disease in Belgium. The OncoSens lab receives $300,000 per annum funding from the SENS Research Foundation and was recently also awarded a $100,000 US grant for continuing their work.  **Dr Haroldo Silva has a PhD in bioengineering from the University of California Berkeley (2012) and has completed the Haas School of Business** Management of Technology Program. Dr Silva has two first author and one second author publications and has presented his work at international and national conferences. His work (PhD thesis) led to the formation of the company, Muscularix Inc. (USA) and Dr Silva is the inventor on three patents. He has received four graduate Fellowships, a **University of California Berkeley** Graduate Award, various undergraduate scholarships and awards.  **David Halvorsen** is a biochemistry undergraduate with industry experience who worked independently in the OncoSENS Lab until he was joined by Dr Haroldo Silva in 2013. David has played key roles in the achievements of the OncoSENS lab, is an inventor on their provisional patent and has given oral and poster presentations of their work in two international conferences. David was awarded a $25,000 US grant to use his work to screen drug libraries for ALT inhibitors. | |
| |  | | --- | |  | | **Research Examples**  Give up to 5 examples of publications in leading Journals demonstrating the translatability of your research. Provide links where appropriate (maximum of 5 pages). (If this is not appropriate to the project you are submitting then write a brief explanation as to why.) | | This project aims to discover drug-like molecules that inhibit the ALT mechanism. The translatability of our project depends on ALT inhibition having the potential to selectively kill ALT[+] cancer cells, without harming normal cells. ALT is not seen in normal human tissue. Henson *et al*. (Henson JD, Cao Y, Huschtscha LI, Chang AC, Au AY, Pickett HA, Reddel RR. (2009). **Nat. Biotechnol.** 27, 1181-1185) has shown that there is no ALT activity in normal cell strains and Bryan *et al*. (Bryan, TM, Englezou, A, Dalla-Pozza, L, Dunham, MA and Reddel, RR. (1997) **Nat. Med.** 3, 1271–1274.) and Heaphy *et al*. (Heaphy CM *et al*. (2011) **Am J Pathol**. 179:1608-15) have shown that there is no ALT activity in normal tissue. Inhibiting the ALT mechanism is known to kill ALT[+] cancer cells. Perrem et al. (Perrem, K., Bryan, T.M., Englezou, A., Hackl, T., Moy, E.L. and Reddel, R.R. (1999) **Oncogene** 18, 3383–3390) showed that genetic repression of the ALT mechanism could cause cellular senescence in ALT[+] cells. Jiang *et al*. (Jiang WQ, Zhong ZH, Henson JD, Neumann AA, Chang ACM, and Reddel RR. (2005). **Mol. Cell. Biol.** 25, 2708-2721) could only study the first suppressor of the ALT mechanism in rare clones of one ALT[+] cell line because suppression of ALT caused death in the vast majority of ALT[+] cancer cells. Together, these studies demonstrate the potential of an ALT inhibitor to selectively kill ALT[+] cancer cells and not normal cells, which do not have an active ALT mechanism. This is consistent with the minimal side-effects seen with inhibitors of the other telomere maintenance mechanism, telomerase (see project rationale and objectives). ALT inhibitors could help the 1.4 million people diagnosed each year with ALT[+] cancers, which includes some of the most difficult cancers to treat, such as pediatric and adult brain cancer, soft tissue sarcoma, osteosarcoma and lung cancers (see project rationale and objectives). |   **Detail the project rationale and objectives** (maximum of 4 pages)  Including design of study, duration, brief description of research topic and its implications on the treatment of cancer. Also include details of the clinical frequency / incidence of this problem in the treatment of cancer. | |
| **INTRODUCTION**  The ALT cancer mechanism provides a novel target for cancer therapeutics, which would potentially benefit both paediatric and adult cancer patients. Our discovery and development of the only biomarker and quantitative assay for the ALT cancer mechanism, the C-Circle biomarker and Assay1, now provides the opportunity to develop the first ALT-targeted cancer therapy. In this project we will undertake the strategy that generally provides the best chance of success, high throughput screening, in which an automated C-Circle Assay will be used to screen a library of 115,000 potential drugs for novel ALT inhibitors. Inhibiting ALT is known to kill or senesce ALT[+] cancer cells without harming normal cells2 and could generate novel cancer therapeutics that have minimal side-effects. Success of this project would integrate well with our research: our development of the C-Circle Assay as clinical test would provide a companion diagnostic for any ALT-targeted cancer therapeutic and any ALT inhibitor would be a useful tool for our studies of the ALT mechanism and the C-Circle biomarker.  **BACKGROUND**  **Telomere Maintenance Mechanisms (TMM) and Cancer.** Telomeres shorten slightly every time a normal somatic cell divides and this eventually prevents any further cell division3. Cancer cells can become immortalised by activating a TMM which counteracts this telomere shortening by synthesising new telomeric DNA from either an RNA template using telomerase4 or a DNA template using ALT5.  **ALT-Targeted Cancer Therapies.** Because the presence of a TMM is an almost universal hallmark of cancer, and repressing these mechanisms experimentally causes cellular senescence or death2, TMMs may be useful targets for new cancer therapeutics. Telomerase-targeted cancer therapies have been reported to have negligible side-effects. ALT-targeted therapeutics are also likely to be highly selective for cancer cells because ALT is not found in normal tissues (Ref. 2, 7 and unpublished), allowing both minimal side-effects and more effective dosing. Conventional therapies do not have satisfactory selectivity for cancer cells and harm normal cells as well, which can limit their ability to achieve a cure and causes serious adverse health effects in survivors, such as sterility, organ failure, secondary cancer and (in children) growth and neurocognitive deficits8.  **ALT in cancer.** Based on the conservative estimate that 10% of cancers are ALT[+]2, there are ~12,000 new cases and 4,300 deaths from ALT[+] cancers annually in Australia8, and ~1.4 million/820,000 globally9. ALT is common in some of the most difficult to treat cancers and median survival for the ALT[+] subgroups in these types of cancers, ranges from one to five years2,10. ALT is relied upon for continued growth and survival in 44% of paediatric glioblastomas multiforme (GBM)7 and 69% of paediatric grade II & III astrocytomas7,11, 60% of adolescent osteosarcomas, 30% of paediatric and adult soft tissue sarcomas (STS)2,10, 24% of adult GBM11 and 5-10% of breast and lung cancers. Although the prevalence of ALT in haematological cancer is unknown, ALT is active in three leukaemia cell lines (unpublished).  **DNA templates used by the ALT mechanism.** Telomeres consist of repetitive DNA with the hexameric repeat sequence being 5'-TTAGGG-3'. Because telomeres all contain the same repetitive DNA, new telomeric DNA can be generated by copying another molecule that contains the telomeric sequence. The telomere being elongated first undergoes the initial steps of homologous recombination with another | |
| telomeric DNA molecule, which can then be used as a template for synthesis of new, single-stranded telomeric sequence12. One of the hallmarks of ALT[+] cancer cells is that they contain large amounts of extrachromosomal telomeric repeat (ECTR) DNA; some of this is linear, and some is circular13. Therefore, there are several sources of telomeric DNA that can be used as the template for ALT-mediated telomere elongation. The template can be another telomere14, a sister chromatid telomere15 or itself (by looping back on itself)15. We speculate that the template can also be linear or circular ECTR, although we have not been able to find any evidence for amplification of circular DNA in ALT (unpublished).  **Assays for ALT.** The ALT mechanism has no known specific enzyme activity, and the presence of ALT activity has often been inferred from detecting telomere-related phenotypes that are characteristic of most ALT[+] cell lines, such as long heterogeneous telomere length distributions or the presence of ALT-associated PML bodies (APBs; PML bodies that contain telomeric DNA)12,16,17. These markers are not entirely satisfactory as they can sometimes give results that are false-positive, false-negative or equivocal. Further, the techniques involved are time consuming and not practical for large numbers of samples or high-throughput applications, and are not suitable for clinical laboratories.  **The C-circle Assay**. We have previously published our discovery of the first ALT-specific molecule, the telomeric C-Circle, and have developed the C-Circle Assay, which has filled the need for a more definitive ALT assay and is also rapidly and linearly responsive to changes in ALT activity1. C-Circles are partially single-stranded telomeric (CCCTAA)n DNA circles and because they appear on activation of ALT and disappear within 24 hours of ALT inhibition, C-Circles may well be an integral part of the ALT mechanism. The C-Circle Assay was sensitive to a few hundred ALT[+] cells and clearly distinguished ALT[+] cells from ALT[-] cells. The C-Circle Assay also gave the correct ALT status for the small number of cell lines in which assays based on phenotypic markers are known to give false-positive or false-negative results. Cancer-derived DNA can be detected extracellularly in blood plasma18, and we found C-Circles in the blood of four ALT[+] osteosarcoma patients1.  **High-Throughput Screening** is often considered the most successful approach to generating new therapeutics. For example, at the Walter and Eliza Hall Institute’s High Throughput Chemical Screening Facility, 58 of 60 high-throughput screens were successful (personal communication, Dr Kurt Lackovic, Facility Coordinator). The use of high-throughput screening for generating ALT-targeted therapeutics is supported by the success of high-throughput screening strategies with ALT’s sister immortality mechanism, telomerase19. Furthermore, we already have proof of principle results that our C-Circle Assay technology can be used to find ALT-targeted anticancer drugs (unpublished).  **Objective**  To discover small molecules that inhibits the ALT mechanism by using the C-Circle Assay for high-throughput screening of a chemical library. These small molecule ALT inhibitors are potential low side-effect anti-cancer drugs that would be applicable 10% of cancer patients, many of whom have poor prognosis with current treatments. It would be part of a subsequent project to advance these "lead" molecules by iterations of chemical modifications and preclinical testing to generate drugs that have maximum potency and bioavailability, minimum side-effects, and to evaluate them for clinical trials. | |
| **Specific hypothesis**  Using the C-Circle Assay for high-throughput screening of a chemical library will discover small molecules that inhibit the ALT mechanism.  **Research design**  **Automated Platform Set-Up:**  The high-throughput version of the C-Circle Assay (**non-sTandard methods**) will be transferred onto the integrated robotics and data management platform at the ACRF Drug Discovery Centre for Childhood Cancer located at the Lowy Cancer Research Centre, UNSW Australia, and managed by AI Dr Greg Arndt. The Drug Discovery Centre will carry out the initial screens on a fee-for-service basis.  **High-Throughput Screening:**  YT-BO is the only ALT[+] glioblastoma multiforme cell line (Ref. 20 and unpublished results). These cells will be grown, harvested and immediately given to the Drug Discovery Centre for automated seeding on 384 well plates. Cells will be treated with the Drug Discovery Centre’s Diversity Compound Library composed of 115,000 highly diverse small molecules covering large pharmacophore space and C-Circle levels quantitated using the High Throughput C-Circle Assay (**non-sTandard methods**). Hits will be validated in triplicate and validated hits have a ten-point dose response determined.  **Evaluation of Hits:**  Validated hits will be tested for their ability to specifically inhibit the ALT mechanism and specifically inhibit the growth and viability of ALT[+] cancer cells. A panel of five ALT[+] and five ALT[-] GBM, lung cancer, osteosarcoma, STS and leukaemia cell lines and five normal cell strains will be used to test the response of cell growth, viability and ALT characteristics to a range of doses. ALT characteristics that will be investigated include a heterogeneous telomere length distribution with a long average telomere length that is maintained over time2 (by Telomere Restriction Fragment analysis), ALT-associated PML Bodies2 and increased telomeric recombination2 (by Chromatin-Orientation Telomere Fluorescence-In Situ-Hybridisation)2, see **non-sTandard methods**.  **NON-STANDARD METHODS**  **High Throughput C-Circle Assay:** Cells in a 384 well plate are incubated in 10 ul NP40/Tween-20 lysis buffer with Qiagen protease at 55oC and then 75oC to inactivate the protease and complete the lysis. C-Circle Assay reaction mix, 15 ul, is added, including dNTPs and Φ29 DNA Polymerase and then incubated at 30°C for 4 hr. C-Circle Assay reaction products are then hybridised to a probe that only produces fluorescence when bound and the fluorescence quantitated using a fluorescent plate reader.  **Terminal Restriction Fragment Analysis:** determines the telomere length distribution in a population of cells and will be performed at various time points over one month (for doses where cells remain viable). Genomic DNA is digested with restriction enzymes that do not recognise telomeric sequence. The fragments are then separated by pulse field gel electrophoresis and the dried gel is hybridised with a telomeric-probe11. | |
| **ALT-associated PML Bodies Assay:** ALT-associated PML Bodies are the subset of PML nuclear bodies that contain telomeric DNA and are detected by combined immunofluorescence with antibodies against PML protein and telomere- Fluorescence-In-Situ-Hybridisation17.  **Chromatin-Orientation Telomere–Fluorescence-In-Situ-Hybridisation**: measures the level of telomeric-sister-chromatid-exchanges in a cell and involves complete destruction of the newly synthesized (BrdU incorporated) DNA strand, leaving the template strand intact for Fluorescence-In-Situ-Hybridisation with telomere strand specific probes that can indicate if a cross-over event occurred after replication between a leading and lagging strand telomere21.  **BUDGET**  The total project budget of $335,000 includes: (i) salary, $100,000 for one dedicated mid-level research staff (ii) consumables, $35,000 for general research (iii) chemical library, $80,000 for a library of 115,000 potential novel drugs and (iv) high-throughput screening consumables, $120,000 for plates and reagents. The project would be run over on year using $200,000 of funds contributed by Tour-de-Cure and $135,000 of funds contributed by the SENS Research Foundation ($35,000 of funds from the SENS would be brought forward from the following year’s funds or the project delayed by four months to accumulate the funding).  **References**  1. Henson, J.D. et al. Nat. Biotechnol. 27, 1181-1185 (2009).  2. Henson, J.D. & Reddel, R.R. FEBS Lett. 584, 3800-3811 (2010).  3. de Lange, T. Nat. Rev. Mol. Cell Biol. 5, 323-329 (2004).  4. Greider, C.W. & Blackburn, E.H. Cell 43, 405-413 (1985).  5. Bryan, T.M. et al. EMBO J. 14, 4240-4248 (1995).  6. Marian C.O. & Shay J.W. Biochim Biophys Acta. 1792, 289-96 (2009).  7. Heaphy, C.M. et al. Am. J. Pathol. 179, 1608-1615 (2011).  8. Australian Institute of Health and Welfare & Australasian Association of Cancer Registries. Cancer in Australia: an overview, 2012. Cancer series no. 74. Cat. No. CAN 70. (2012).  9. Ferlay J. etal. GLOBOCAN 2012 v1.0, International Agency for Research on Cancer (2013).  10. Lee Y.K., Park N.H., Lee H. Int J Gynecol Cancer. 3, 434-441 (2012).  11. Henson, J.D. et al. Clin. Cancer Res. 11, 217-225 (2005).  12. Henson, J.D. et al. Oncogene 21, 598-610 (2002).  13 Nabetani, A., Ishikawa, F. Mol Cell Biol. 3, 703-713 (2009).  14. Dunham, M.A. et al. Nat. Genet. 26, 447-450 (2000).  15. Muntoni, A., Neumann, A.A., Hills, M. & Reddel, R.R. Hum. Mol. Genet. 18, 1017-1027 (2009).  16. Bryan, T.M. et al. Nat. Med. 3, 1271-1274 (1997).  17. Yeager, T.R. et al. 59, 4175-4179 (1999).  18. Tsang, J.C. & Lo, Y.M. Pathology 39, 197-207 (2007).  19. Bernardes de Jesus, B. et al. Aging Cell. 4, 604-621(2011).  20. Sampl, S., et al. Transl Oncol. 1, 56–65 (2012).  21. Bailey, S.M. et al. Science 293, 2462–2465 (2001). | |
| |  | | --- | | **Is there any opportunity for this grant to receive matching funds or any additional funds from other sources resulting from funds received from Tour de Cure? If so, please provide details.** | | Tour-de-Cure funds will suffice to initiate a formal collaboration between the applicant’s lab and the OncoSens Lab at the SENS Research Foundation, California, USA. Once the collaboration is activated, the SENS Research Foundation will contribute up to $US100,000 per year to the collaboration. |   **Detail any collaboration involved in the research project or forecasted collaborative benefits of the results** (maximum of 2 pages except for Collaboration Research Grant which is up to 6 pages) | |
| This research project will involve two collaborations   * + 1. The OncoSens Lab, SENS Research Foundation, USA. Dr Henson’s (the applicant’s) lab and the OncoSens Lab have had an informal collaboration over the last two years. This collaboration has involved sharing of tasks, knowhow, knowledge and resources, which has resulted in an advancement to the C-Circle Assay. This advancement is subject to a provisional patent (in preparation) and allows the C-Circle Assay to be automated for high-throughput screening, which is the key to this project. The advancement may also allow commercialisation of the C-Circle Assay as a research kit and clinical diagnostic. For this project Dr Henson’s lab and the OncoSens lab will enter into a formal collaboration agreement, which will see both labs work as one lab under the leadership of Dr Henson. This will allow both labs to function as one optimally resourced lab and maximise the synergy of the collaboration, along with other benefits of collaborating, such as widening access to expertise, human resources, equipment, infrastructure, networks and funding opportunities.     2. Dr Greg Arndt, ACRF Drug Discovery Centre for Childhood Cancer (located in the same building). This project will initiate a collaboration with Dr Arndt and his Unit, who have the experience and infrastructure required for the high-throughput automated screen that will be vital not just for this project but also for other aspects of our research program, such as a high-throughput C-Circle Assay screen of siRNA and overexpression libraries to find new gene targets for anti-cancer drugs. Success with this project will also initiate other valuable collaborations at various stages of the translation pipeline. For example, we have had initial consultation with Professor Naresh Kumar, Medicinal Chemistry, UNSW Australia, regarding collaboration for the optimisation of any identified anti-cancer drugs. | |
| **Detail any other funding that the project currently receives or is seeking to access** | |
| Dr Henson Receives fellowship funds from the Cancer Institute NSW that will support his involvement in this project. Support for this project has also been sought from the Cure Brain Cancer Foundation. | |
| **Details of the best contact for the Research Advisory Committee to contact regarding the details of the research project** | |
| Name: | Dr Jeremy Henson |
| Phone: | (02) 9385 3205 |
| Mobile: | 0430 448 579 |
| Email: | j.henson@unsw.edu.au |
| **Please provide copies of the following information with your application**   * + 1. Ethics proposal and approval   This study does not require ethics approval.   * + 1. Most recent audited financial statements/results   Please the annual financial report for UNSW Australia at: <https://www.fin.unsw.edu.au/OurServices/FinancialControl_FinancialAccountingReporting_AnnualReports.html> | | |
| **A significant part of Tour de Cure is based on Team Members raising funds. Please detail how your organisation can support Tour de Cure in recruiting team members in the future to its tours. (Note team members include riders, guest riders and support crew)** | | |
| UNSW Australia is a prospective source of team members. The applicant would be delighted to assist with setting up stalls and informative advertising on campus, to recruit team members and support. | | |

**Your Application for a research project is now complete. PLease send an email to** [**jim@tourdecure.com.au**](mailto:jim@tourdecure.com.au) **with the application and any supporting documentation.**

# Further information

For further information on Tour de Cure or in relation to the Expression of interest forms then please do not hesitate to contact the following Tour de Cure team member -

**Jim Hollier**

*Finance and Operations Manager*

*Tour de Cure*

**M: 0412 256 542**

**E:** [**jim@tourdecure.com.au**](mailto:jim@tourdecure.com.au)

Alternatively you can visit our website:

[www.tourdecure.com.au](http://www.tourdecure.com.au)