



FINAL WAMSI PROJECT REPORT

Instructions for Use: Please complete each of the sections below and return to (insert Node Science Coordinator's name/Node Leader's name and email contact details in order to enable scientific verification of the report prior to it passed on to the WAMSI HQ). The project report template tries to cover all the major facets of reporting that are required. There is some flexibility in how this proforma is completed, based mainly on the size of the project and whether there are a number of discrete sub projects. For example, if the project is quite small and has a single, simple methodology, then complete sections 3, 4, 5, etc. If the project has multiple discrete sub projects, then complete section 2 as this enables discrete research chapters to be written. Discussion, acknowledgements and references can be combined if the project sub components being reported on are related and cross reference one another. In the situation where the sub project components are very different, then the discussion, acknowledgements and references will need to be kept as discrete entities as they relate to that particular sub project. If there is any clarification required, please don't hesitate to contact the WAMSI HQ staff.

Project Details

Project Number and Title:	WASMI Node 5 Project 2 Biomolecular Diversity and Partnered Biodiscovery
Node Leader:	Howard Shawcross
Project Leader:	Prof Peter Leedman
Project Team:	Prof Peter Leedman (WAIMR), Viki Russell (WAIMR), Dr Jane Fromont (WAM), Prof Chris Battershill (AIMS), Dr Libby Evans-Ilidge (AIMS)
Project Start Date:	1 July 2008 (delayed until late 2010 due to Regulatory issues, when a 179 approval finally granted)
Project End Date:	30 July 2011, but realistically will be later due to the very long delay in gaining sample access, as we progress the screening into compound detection, isolation and characterisation.
Due Date for Final Report:	
Project Funding:	
WAMSI	\$
Additional Cash	\$
Additional In-Kind	\$
Total Funding	\$

1. Project Objectives and Achievement Criteria

Confirmation of the project objectives and the delivery of milestones against the Key Performance Indicators:
Milestone 5.2.1.1 Collaborative Research Agreement amongst WAIMR, AIMS, WAMSI, UWA signed
Milestone 5.2.1.2 Year 1 "NCI" target extracts delivered to WAIMR (n=10) Due to regulatory issues and extraordinary delays in obtaining a 179 Approval from the Department of Fisheries, we received the compounds late in 2010, instead of in 2008.
Milestone 5.2.1.3: Screens on amplified extracts/compounds performed in late 2010.
Milestone 5.2.1.4: Isolation/verification of hits – in progress currently
Milestone 5.2.1.5: Structure confirmation – not achieved
Milestone 5.2.1.6: Decision point meeting and project plan for funding leads, including IP assessment. – not achieved

Milestone 5.2.1.7: Progress based on acquisition of external funding – not achieved

Milestone 5.2.1.8: Public seminar/workshop – not achieved

2. Research Chapter(s)

This section should make up the bulk of the report and may include more than one chapter where there are a number of sub-projects that are contained within one project. The section should include the following subheadings for each project/sub-project.

- a) Introduction
- b) Methodology - further details provided below in (3)
- c) Results - further details provided below in (4)
- d) Discussion - further details provided below in (5)
- e) Acknowledgements
- f) References

3. Methodology

Summarise the method(s) utilised as part of the project and provide a listing of the sub-projects (if appropriate). Sub-project reports should be provided as annexures to this project report.

The goal of this very interesting biodiscovery project was to perform proof-of-principle studies on a carefully selected group of marine samples in order to identify ones that have novel anticancer properties. This is an area of significant interest world-wide, as some marine-derived compounds are now entering early phase clinical trials in patients with cancer. So the precedent is a good one, and as WA has such unique and diverse marine organisms, the project holds great promise.

However, the major issue in this node was the YEARS of DELAY in actually obtaining access to the samples, due to regulatory issues. Thanks to excellent work from the node leader Jason Froud, this approval was finally granted in late 2010 (over 2.5 years late).

Fifty compounds isolated from up and down the WA coast were carefully selected by Prof Battershill and Dr Evans-Illidge for potential anticancer activity based on an intimate knowledge of the marine organisms and Prof Battershill's experience in the mining of other organisms with a collaborator at the NIH in the USA.

These samples were provided by AIMS to Dr Jane Fromont from the WA Museum, who then delivered them to the Leedman laboratory in WAIMR (Western Australian Institute for Medical Research) as freeze dried preparations. They were then dissolved predominantly in methanol and used in cell proliferation assays to determine the IC50 of growth inhibition of two different human cancer cell lines (LNCaP, human prostate cancer; MCF-7, human breast cancer).

4. Results

Present the results of the project and attainment of scientific objectives. Assess the success of meeting each objective identified in the proposal, as initially approved or later modified. For each objective:

1. Re-state the objective,
2. Tell the degree to which it has been met, and
3. Describe the technical findings and conclusion in a paragraph or two.

1. Objective

Milestone 5.2.1.3: Screens on amplified extracts/compounds performed in late 2010.

2. This objective was met completely, as all 50 extracts were screened on two human cancer cell lines and the data on IC50's was determined.

3. Findings and conclusion

We found that a significant number of samples had anticancer activity with IC50s of 0.3-10 micromolar

range, which from crude extracts is an exciting finding. Interestingly, there are samples with strong activity against prostate cancer and not breast cancer cell proliferation, and vice versa. In addition, we found two samples with activity against both cell lines.

These data are exactly what we would have hoped for, starting from crude extracts, and obtaining some very good hits. These positive hits are now going to be subfractionated by our collaborating chemist, who will provide the Leedman lab with another set of extracts to test for retained activity, before we progressively perform iterative rounds of purification and activity testing (usually about 4 rounds) until we arrive at a pure compound.

Conclusion: The extract screening of 50 crude WA marine compound extracts against human breast and prostate cancer cells has revealed a few very exciting "hits" that may, upon further iterative rounds of purification and testing, reveal novel anticancer compounds.

5. Discussion

Implications for Management and Advancement of the Field – Describe the key findings as they relate to the objectives and the management questions discussed at the outset of the project.

This project is predicated on the belief that the marine organisms of the WA coast will contain substances that may be active against human cancer cells. This is based on data from studies around the world, where marine substances are now in clinical trials, and may provide new therapeutic strategies for cancer treatment.

Based on the vast array of novel marine organisms in WA, it is hoped that a similar outcome might eventuate from screening of our extracts.

Certainly, the preliminary data is exactly what we would have liked, establishing a strong basis for further rounds of purification and screening to establish the identity of one or more novel anticancer compounds.

These proof-of-principle studies validate the approach and emphasize the need to progress the work as fast as possible.

Problems encountered (if any) – Describe any major problems/issues encountered during the study and how they were addressed.

This project has suffered from massive delays due to Regulatory issues. We waited literally several years to obtain approval from the Department of Fisheries. Once obtained, we have generated novel information, that will hopefully lead onto further identification of novel anticancer compounds.

New Research Directions (if any) – Identify new research directions pursued during the course of the project and reasons for modifying original research plans. Describe how the changed research agenda improved the project.

There are no new directions, only exciting data from our initial screen that suggests we have several initial hits and that subsequent rounds of iterative screening need to progress forthwith and hopefully novel compounds identified that may have a market and potential IP capture.

6. Overall Project Accomplishments

Students supported – Record the name of each student involved with the project. Indicate whether PhD

or other (give details) and briefly describe their role.
Nil
PhD theses, Dissertations and Student Placement – Please give complete citation for theses and dissertations (student's name, month and year completed or expected, level of degree, institution). Please provide a copy of the abstract of the thesis or dissertation when complete.
Nil
Publications - List in standard academic format the citations of literature produced during the reporting period. Include journal articles, book chapters, reports, etc. submitted, in press and printed. Please provide a paper and electronic version copy of each publication resulting from the project. If there is a link to the journal electronically, please also include this.
Nil to date, we would need further purification and characterisation of the pure anticancer compound prior to publication.
Presentations - Cite any presentations resulting from the project, including conferences, symposiums, etc.
WAMSI symposium, but no others as the data is not yet advanced enough. Hopefully that will change soon.
Other Communications Achievements - Interviews, press releases, etc.
Nil

7. Overall Project Benefits Please note: Benefits go beyond Results and Accomplishments to provide information on direct physical, environmental, economic or social gains realised as a result of a research project or outreach activity.

Discovery and Application of New Products and Processes (if applicable) - Describe any actual or anticipated products or processes discovered or developed in the project.
As stated above, if the preliminary data leads onto discovery of novel anticancer compounds, there are potentially very significant IP surrounding their activity in a cancer context.
Tools, Technologies and Information for Improved Ecosystem Management - Describe how project results are being (or will be) translated into sustainable use and management of coastal and ocean ecosystems. Tools might include benthic habitat maps or environmental sensitivity indicators. Technologies might include remote and bio-sensing, genetic markers, and culture systems. Information might include technical assistance, training and educational materials.
N/A

Forecasting for Natural Resource Management Decisions - Describe how results already are being used - or are expected to be used after project completion - by natural resource management to make decisions based on project forecasts. Forecasts may be due to field and laboratory studies and models. Examples include hypoxia forecast models, algal bloom alerts, forecasts of fishery harvest, and prediction of impacts from ecosystem stressors such as pollutants or invasive species.

N/A

Impacts - Impacts are higher order, usually long-term results of a project's activities that have significant scientific, economic or social benefits. Impacts may involve behavioural, policy or economic changes. Describe impacts (anticipated or realized). These impacts may involve behavioural, policy or economic changes. Seminal contributions to science are considered impacts especially if the research findings lead to major progress in a particular field, implementation of new technologies or have a substantive bearing on an economic or societal issue.

If we were to discover that one or more of these extracts contain a novel anticancer compound it could have major implication for cancer therapeutics globally.

8. Project Metadata and Data Generated

These must be available at an open access repository/data centre/iVEC.

<http://waodn.ivec.org/geonetwork/srv/en/metadata.show?uuid=0f44986b-2a52-4586-a613-c8de2c4102a4>

9. Linkages to Associated Projects – can be WAMSI and non-WAMSI

Node 5.2 is linked with Dr Jane Fromont at the WAM as she has curated and provided the samples from her repository.

10. Other Comments and General Discussion

Our exciting preliminary data generated after massive delays (out of our control) provides a strong foundation for continued work in the area and iterative rounds of purification and activity testing. We hope to pursue the work in the next year to achieve the original goals outlined in the WAMSI project.

11. Annexures

- **Sub-project reports presented**
- **Additional attachments**