



OGIRC

Ontario Ginseng Innovation & Research Consortium



ANNUAL REPORT

April 2010 - March 2011



*This report is available as a PDF file from the OGIRC website at
www.uwo.ca/ogirc/governance*

I. Overview – Year 3 April 2010 – March 2011

The OGIRC was established in April 2008 and this report covers our accomplishments and the challenges encountered in the third year of operation. The overall goal of OGIRC is to employ a multi-disciplinary approach involving academia, government and private sector partnership to use state-of-the-art technologies for Ontario ginseng agriculture and product development. For this, three major studies have been proposed: i) systematic evaluation of ginseng product quality, ii) development of superior Ontario ginseng cultivars for agriculture, and iii) production of value-added products by advanced processing.

Progress of Project

The multi-sector based research has proceeded according to plan with full participation of all partners. The interdisciplinary and collaborative effort and spirit of the group were fully realized in year 3 with scientists from different backgrounds truly working as a team and trainees recognizing and appreciating the interdisciplinary nature of the program. In addition, the reputation of our research and researchers has attracted new industry collaborators who have who have widened the scope and depth of our research by providing state-of-the-art technologies, resources and potential opportunities for new funding and further collaboration.

Study #1 has been successful with attainment of all milestones and the generation of top quality and important research findings. There is a better understanding of this multi-action herb, with effects ranging from immunomodulation, anti-infective activity, stimulation of adipocyte metabolism, protection against vascular injury and early atherosclerotic lesions, ischemia–reperfusion injury, heart failure, metabolic stress, erectile dysfunction, metabolic syndrome and diabetic complications. In addition, the elucidation of some of the mechanisms of action has provided a sound scientific basis to explain the purported beneficial health effects of North American ginseng. Our research findings will also provide the scientific basis for promoting Ontario-grown ginseng by the growers and the translation into new use. In the context of the overall research project, these findings will provide new endpoints for evaluating product quality, direction for developing new value-added products and selective ginseng cultivars for these important health effects. However, we do have to face the challenge of deciding which area(s) or medicinal effect(s) to focus on for possible commercialization, cultivar development and design of value-added products.

The objective of Study#2 is to develop a unique (protectable and trackable) ginseng variety with predictable quality, safety and medicinal properties. This is a novel approach involving experts in plant biotechnology and agriculture, chemistry, pharmacology and toxicology. The milestones of Study#2 were attained in Year 3 except the genomics analysis which was delayed due to technical difficulties which have since been resolved. Clonal lines have successfully been developed using micropropagation technology, and bioreactor-based scale-up production and protocol for cryopreservation of ginseng germ lines are in place. It is expected that substantial advances will be made in the characterization of the clonal lines in the next year. One of the limiting factors appears to be the resources for evaluating the medicinal potency of the clonal lines.

The objective of Study #3 is to produce innovative value-added ginseng products. In year 3, the primary goal was to develop technology to extract bioactive constituents for pharmaceutical development and to investigate new delivery systems for ginseng (ginseng-based angiogenic bone cements for bone healing, yogurt-based ginseng, and micronized ginseng extracts are some examples). The engineering technology for this is available, but the success of this study depends on a strong interaction with other disciplines: e.g. phytochemistry and pharmacology. Stronger collaborative efforts are being encouraged and developed.

Education/training/outreach. The OGIRC continued to expand and enhance this facet of its program throughout Year 3 with ongoing recruitment of post-doctoral fellows, graduate students and technicians. Education and training activities for our HQP and investigators included six Journal Clubs; a summer retreat with special presentation on moving from bench to bedside and intellectual property management; and a joint OGIRC/CICMR conference that offered training and workshop sessions for trainees and an Advanced Processing workshop. An interdisciplinary focus is embodied in all educational sessions. OGIRC again participated in the Royal Agricultural Winter Fair with an exhibit and oral presentation for health professionals.

Administration and management. The central office continued to function at full capacity and took advantage of the work study program to distribute the work load and provide students with additional training opportunities. The office managed the daily operations of the project: budgeting and audit activities, monitoring of accounts, coordinated meetings, established sub-grant agreements, registered trainees, coordinated education, conference and outreach activities, grant submissions and facilitated agreements. As efficiencies are gained, the office continues to plan new initiatives in the upcoming year.

Impact

The multi-disciplinary research approach used and the scientific excellence of the participating researchers in this project represent a major step forward in advancing the science of traditional medicine, as evidenced by a feature article in Toronto Star in 2011. The successful outcome of our research, based on a multi-sector approach covering all aspects of the R&D of herbal medicines, has provided leadership in this area of research. Moreover, our research model is in line with the new vision of AAFC that emphasizes the role of agricultural bioproducts in human health. This successful partnership will bring together many synergies in the near future.

i. Scientific community.

We have generated significant amounts of high quality results in support of the recent interest in the potential health benefits and modernization of traditional medicines. This is evidenced by four of our scientists being invited to deliver oral presentations at the International Ginseng Conference in Korea and another scientist being recognized for an outstanding poster presentation.

ii. Agriculture.

Encouraging outcomes from Studies 1 and 2 will have a significant positive impact on Ontario ginseng growers. Our research will provide, for the first time, a strong scientific base for their marketing strategy in terms of product quality, efficacy and safety. Although the cultivar development study has a longer time frame, some of the technology developed, e.g. tissue culture and micropropagation with scale-up production capability, could find application in ginseng agriculture in the near future

iii. NHPs industry, regulations and health care.

Our preclinical studies have yielded very promising results in terms of the benefits of ginseng on immune function, bacterial infection, cardiovascular health, metabolic syndrome, diabetic complications, and erectile dysfunction. Observations based on in vitro and in vivo data will require validation in human studies. However, our mechanistic understanding of the action of ginseng will provide the biological plausibility for its purported health effects in humans. This will contribute to the overall evidence to support health claims for registration or licensing of NHPs in Canada. In addition, the wide range of medicinal properties that we have reported will encourage the NHPs industry to apply for non-traditional health claims under the Canadian NHPs Regulations. This will significantly expand the domestic market for Ontario ginseng.

iv. Ontario.

In addition to the potential direct impact of our research outcomes on the Ontario bioeconomy via the improvement in the ginseng agricultural practice and the expansion of the domestic and international ginseng market, there will be spin-offs. The successful recruitment and training of HQP with interdisciplinary experience and skills together with the engagement of significant numbers of high profile researchers in five research-intensive universities and AAFC will build a critical mass which could markedly enhance Ontario's R&D capacity in the nutraceutical/functional food industry

II. Research Report Summary– April 2010 to March 2011

(from Report to Governance Committee May 10, 2011)

Overall Objectives and specific goals of Year 3 Multi-disciplinary research is organized into Platform Technology Groups (PTGs), the work of which is described in the individual PTG leader reports (see Appendix D). The summary of the research report will be concerned with the progress of the consortium as a whole in attaining the specific research goals of Year 3. This will include the contribution of private sector partners.

Study 1: Systematic Evaluation of Product Quality of North American Ginseng Cultivated in Ontario

Progress to date suggests that we have been successful in demonstrating how a multi-disciplinary and integrative project could be achieved via a platform technology group concept coupled with strong Central Office and institutional supports. We have also demonstrated that a highly integrated project that depends on contributions from academia, government and multiple private sector partners is achievable.

In this study, 4 year-old ginseng roots sampled from five farms were provided directly from the Ontario Ginseng Growers Association (OGGA) (designated as H0) in 2008 or they were harvested from nine farms (H1) under the guidance of OGGA by D. Brown of Agriculture and Agri-Food Canada (AAFC) in 2008. In 2009 and 2010, two additional harvests, H2 and H3, from 10 farms were completed. This will provide sufficient samples to evaluate farm to farm and year to year variability in the quality of Ontario-grown ginseng for the duration of this project. In year 3, the phytochemical analysis of H1 samples, showed significant farm to farm variability in ginsenoside levels, which was similar to those reported in Year 2 for H0 samples. However, the year to year variability in the mean ginsenoside levels was insignificant. This data suggested that branding of 4 year-old Ontario-grown ginseng roots based on individual farms would be very difficult in light of the farm to farm variability. However, blending of sufficient quantity of ginseng from different farms to produce “standardized” products may be a solution. Additional study with H2 and H3 ginseng will validate our current finding.

In addition to the standard HPLC analysis for ginsenosides, the Phytochemistry group has developed a NMR metabolomics method for the characterization of ginseng extracts. Our new industry collaborator, AB SCIEX, has also provided their state-of -the-art LC-MS/MS metabolomics expertise in characterizing our ginseng extracts. This will enhance our capability to evaluate product quality. The other major phytochemical constituents of ginseng are the polysaccharides. There are many challenges in their analysis. A new HPLC-ELSD method has been developed by the Phytochemistry group to measure the monosaccharides from hydrolysed ginseng components. The monosaccharide composition has been determined and the data provides insight into the types of polysaccharides which are found in American ginseng. Different ginseng polysaccharide components have been isolated by chromatographic techniques for further characterization by the Preclinical Studies group. It should be noted that the phytochemical profile alone is insufficient to evaluate product quality, because the exact bioactives that mediate the medicinal effects of ginseng are poorly defined. Accordingly, it is important to determine

whether the observed farm to farm variability in ginsenoside level could be translated into differences in medicinal potency.

One of the exciting accomplishments of Study #1 is the demonstration with state-of-the-art methodologies of the wide range of significant and relevant medicinal properties of the two types (aqueous and alcoholic) of Ontario-grown ginseng extracts. Our collaboration with the scientists from AB SCIEX has also allowed us to incorporate metabolomics in studying the pharmacology of ginseng. This will provide good evidence for the licensing Ontario ginseng as natural health products with non-traditional health claims under the new NHPs regulations of Health Canada; which in turn will have a significant positive impact on the NHPs industry and Ginseng agriculture.

The other important and novel finding is that the observed medicinal effects of ginseng are extract-specific. The aqueous extract was associated with immunostimulation, anti-infective activity, stimulation of adipocyte metabolism, protection against homocysteine-induced vascular injury and early lesion of atherosclerosis as well as metabolic stress and erectile dysfunction in diabetes, while the alcoholic extract was anti-inflammatory in nature and protected against ischemia-reperfusion injury, heart failure and metabolic syndrome as well as diabetic complications. We are the first to define the yin and yang action of ginseng as it is related to the paradoxical effect on immune function. It appeared that this action may be extended to other activity of ginseng. Our study may lead to the identification of novel bioactive chemical components of ginseng and the development of more specific ginseng products. The finding on the extract-specific pharmacological effect has significant implication in the manufacturing, production, development and regulation of ginseng extract based products as well as their safe and appropriate use by consumers.

This extract-dependent pharmacological activity is mostly likely related to their unique phytochemical characteristics. Since polysaccharides are unique to the water extract, their role in mediating some of the medicinal effects will be examined in year 4 and the technology developed for polysaccharides analysis will be very useful.

Our Study #1 in Year 3 has contributed to a better understanding of this multi-action herb and has provided a sound scientific basis to explain the purported beneficial health effects of North American ginseng. This will provide new endpoints for evaluating product quality and, more importantly, provide direction for developing new value-added products and selective ginseng cultivars for these important health effects.

Study 2. Ontario Ginseng Cultivar Development.

Activities of the Plant Biotechnology group were on two Project objectives: (1) To provide a systematic evaluation of the quality of Ontario-grown ginseng roots and to develop criteria for certification/branding of Ontario ginseng (which has already been covered in the above) and (2) To develop a unique (protectable and trackable) ginseng variety with predictable quality, safety and medicinal properties.

Substantial progress was made on four fronts; namely, in the area of development of a liquid-based micropropagation system, development of a cryopreservation protocol, constituent analysis of developing three year old roots and 1 and 2-year-old clonal lines and nucleic acid sequencing of expressed genes working towards genetic markers.

In the liquid-based micropropagation system, a rapid and highly efficient method has been developed. A significant improvement in the growth of explant resulted from the reduction of in the phenolic content which increases in cultures over time and inhibits proliferation. In the improved protocol, single nodes were cultured in liquid medium containing an optimized complement of 2.5 mg/l kinetin, 0.5 mg/l NAA and 50 mg/l activated charcoal. A reduction in phenolic production, increased antioxidant capacity and greater shoot proliferation were observed with activated charcoal and melatonin, polyvinylpyrrolidone and ascorbic acid added to the liquid culture medium. This is the first report of a direct organogenesis production system from single node segments (manuscript submitted) in ginseng.

An efficient method for cryopreservation of ginseng cultivars has been developed using shoot tips. The maximum regrowth (60%) of shoot-tips cryopreserved in liquid nitrogen occurred after three weeks of cold acclimation and pretreatment on sucrose (0.3M) or a combination of ABA (0.1M) and sucrose. Shoot tips showed normal development and cotyledons produced embryogenic callus after the cryopreservation process. This is the first report on cryopreservation of shoot tips and cotyledons of *Panax* species and provides a safe long-term storage method for improving the security of ginseng germplasm.

A wide range of ginsenosides, anti-oxidant activity and immunostimulatory activity were identified in 30 clonal lines. Component contents and ratios varied between 5 and 10 fold in the lines tested. There was no apparent correlation between lines and their respective contents and of ginsenosides, phenolics, antioxidant activities or immuno-stimulatory response in the first set of tested lines. This suggests these traits are not genetically linked and can be individually screen and selected. This also confirms the view that field-sourced variability can be controlled, reduced and specific traits can be selected for to produce specialty targeted lines with specific enhanced efficacies (e.g., high ginsenoside content, higher immuno-stimulatory activity).

Methodology was developed for extracting and sequencing RNA (in cooperation with Andrew Sharpe, PBI, Saskatoon) from developing ginseng roots. Seven developmental stages covering the growing season have been sampled and sequenced. The reference genome for Single Nucleotide Polymorphisms (SNPs) as genetic markers is presently underway.

Study 3. Value-added Ginseng Products

This study is being undertaken by the Advanced Processing Group (APG) with participation of the Phytochemistry Group (PG) as well as the Preclinical Studies Group (PSG).

One of the overall objectives was to develop innovative methodologies to extract bioactive constituents including ginsenosides and polysaccharides for pharmaceutical development. The objectives of this year for the OGIRC project were to further examine our novel extracts isolating active components from

ginseng roots including fractionating polysaccharides and acetylated ginsenosides (P. Charpentier). Analysis of these components was undertaken using several techniques including supercritical fluid extraction (SFE), ultrasound assisted extraction and Soxhlet extraction. In addition, a goal has been to setup a supercritical fluid chromatography (SFC) unit for the separation and analysis of various components from ginseng root for further study by the pre-clinical researchers. Bio-assay studies were focused on in the past year of these novel materials examining their immunological and angiogenic activity (in collaboration with E.Lui).

The second objective was the development of delivery systems for ginseng bioactives.

- 1). Preparation of ginseng-based bone cements used in cemented arthroplasties. Angiogenic ginsenoside, Rg1, which is also known to have anti-apoptotic activity will be used to produce cement that would benefit wound healing. (Charpentier & Lui).
- 2) A preliminary study just got underway concerning the production of ginseng-based probiotic yogurt as a delivery system and production of NHP with enhanced immunostimulatory or anti-inflammatory properties. This is an interdisciplinary project involving a pharmacologist (E Lui), microbiologist-immunologist (G Reid), and a food scientist (S. Hemkat, Brescia College) with potential collaboration with a private sector (Danone). Members of the Advanced Processing Group may be involved at a later stage to provide different dosage form of ginseng.
- 3) The other area of focus was the production of ginseng extract formulations for oral administration with different dissolution rates (J Zhu). A spray drying method was used to produce fine dry powder from ginseng extract. The dissolution and ginsenoside release rates have been determined to be predictive of in vivo behavior. The bioavailability and efficacy of this formulation will be tested by the preclinical group in Year 4.

Safety study group.

Ginseng has a long history of use in humans and it has generally little safety concerns. However, there is a safety concern with the development of ginseng cultivars study (#2). It is uncertain whether these cultivars would have excessive risk to the consumers in view of the fact that they are selected for their high degree of specificity in biological or medicinal effects or potency. There are two areas of concern: 1) the adverse effect on pregnancy; and 2) interaction with drug metabolism. Most natural health products are not recommended during pregnancy primarily because of insufficient safety data. Tests of exposure to ginseng extracts (aqueous/hydroalcoholic) on mouse preimplantation development in vitro have now been completed. The aqueous ginseng extract (but not the alcoholic extract) induced a concentration dependent inhibition of preimplantation development in vitro. This in vitro result will be validated by using more pharmacologically relevant conditions. 2) The initial and most important step of drug metabolism is oxidation by a member of the family of Cytochrome P450s (CYPs). The specific enzyme, CYP3A4, is particularly essential. It contributes to the inactivation and elimination of an estimated 50% of all drugs. Majority of the samples examined thus far (H0 and H1 harvest) were devoid of inhibitory activity on 3A4. Similar protocol will be used to evaluate newly developed ginseng cultivars for safety evaluation in the future.

Research Capacity Development

At the end of Year 2, there were eighteen senior investigators who received OGIRC funding, and a total of ten PDFs, eleven graduate students, and five part-time technicians. Over the last year, there has been a steady increase in personnel with the addition of 8 new collaborators (one with funding from OGIRC), 8 additional PDFs, an increase of 9 graduate students to make a total of 20, while maintaining the number of part-time technicians. Our program has been very popular with undergraduate students (as volunteers or work-study students) with a surge of 16 in year 2 to reach a total of 48.

In year 3, we were also successful in establishing new partnerships with the industrial sector.

1. AB SCIEX is a global leader in the development of best-in-class technologies that help answer complex scientific challenges and improve our world. It “creates scientific instrumentation, software and services for the life sciences, clinical research and industrial markets, empowering our customers with technologies that are used in drug discovery and manufacturing, food and environmental safety, and clinical research.” With a more than 20-year history of innovation and market leadership under the Applied Biosystems/MDS Analytical Technologies joint venture, it is now operate as AB SCIEX, a new company within the Danaher Corporation. AB SCIEX has been collaborating with DR Lui of OGIRC since July 2010 in conducting metabolomics study on ginseng product quality and its pharmacological effects in animal models.
2. The Danone group is a world leader in dairy products and probiotics, with a turnover exceeding \$20 billion, and over 1200 scientists in R&D. Collaborative research is under discussion with E. Lui with the intent of incorporating ginseng in probiotic yogurt.

III. Highlights of Year 3

1. *Submission of the Year 2 ORF Progress Report to the Ministry of Research & Innovation
June 4, 2010*

The second Annual Progress Report was submitted by the Ontario Ginseng Innovation & Research Consortium (OGIRC) to the Ontario Ministry of Research & Innovation on June 4, 2010, having received prior endorsement by the OGIRC Governance Committee. The report provided a comprehensive background and rationale of the formation and composition of the OGIRC; a detailed description of its research progress to date and future plans; measurements of research capacity building (HQP recruitment); a list of the publications and presentations made by OGIRC researchers and their knowledge translation and youth/public outreach initiatives. Thank you to our researchers and trainees for their diligent efforts in compiling this information.

2. *2010 Summer Retreat “Fostering a Multi-disciplinary Research Environment”
June 15, 2010*

The 2010 OGIRC Summer Retreat was held on June 15 in the St. James Auditorium of Brescia University College, UWO. The Retreat’s objectives were to enhance the interdependence of the Platform Technology Groups, provide details on outreach and communications initiatives and solicit ideas for trainee learning enrichment and workplace readiness. Guest speaker, Dr Simon Chiu, a psychiatrist from St Joseph’s Regional Mental Health Centre, described moving from pre-clinical to clinical studies in “Translational Research: from Bench to Bedside.” Mr Paul Paolatto, Executive Director of WORLDiscoveries offered insights into intellectual property and commercialization issues in his session, “Intellectual Property: co-authorship, co-inventorship and patents.” These two sessions were highly rated in participant feedback. Trainees indicated a greater appreciation for the interdisciplinary nature of the project, and a real sense of being heard in the Retreat discussions. Our thanks to WORLDiscoveries for their sponsorship and participation in this educational retreat.

3. *2010 OGIRC Annual Conference, “Production, Pharmacology and Health Benefits of Traditional Medicines”*

October 23 – 24, 2010, Ottawa, Ontario

The OGIRC 3rd Annual Conference was held on October 23 and 24 Lamoureux Hall at the University of Ottawa campus. During the conference, the OGIRC met to share research progress, introduce new collaborators and provide trainees with an opportunity share their research findings in an oral or poster presentation format. The conference was well-attended, gathering over 125 attendees from academia, other research institutions and industry to discuss Plant Biotechnology, Agriculture & Phytochemistry; Pre-Clinical Studies; Metabolomics; Advanced Processing; and Commercialization. The plenary lecturer was Dr. Yung-Chi Cheng, Professor, Yale University and Chairman, Consortium for Globalization of Chinese Medicine (CGCM) discussing “Potential, bottlenecks and approaches to develop future medicine based on traditional Chinese medicine”.

Highlights:

- Oral and posters presentations from OGIRC members, invited speakers and external contributors

- Trainee oral presentations – Graduate Student Awards: Melissa Moey, UWO & Martha Mullally, U Ottawa; Post Graduate Award – Cory Harris, McGill U
- Trainee poster presentations - Awards to: Undergraduate - Cheryl Lui, UWO; Graduate - Chieu Ta, U Ottawa; Brendan Walshe Roussel, U Ottawa; Despina Harbilas, U Montreal; Post Doctoral – Ester Uchendu, U of Guelph
- Graduate Student Workshop on NHP regulations

4. *2010 Royal Agricultural Winter Fair,*

November 5 – 14, 2010, Toronto, Ontario

The Ontario Ginseng Innovation & Research Consortium (OGIRC) exhibited in the Royal Agricultural Winter Fair's "Health Professionals' Salon in the "Journey to Your Good Health" exhibit. The Royal is the largest indoor agricultural fair in the world and attracts more than 340,000 participants and visitors each year. The "Journey" is a major exhibit at the fair that promotes the foods grown by local farmers and the latest trends in functional foods to 22,000 plus visitors.

The objective of the exhibit was to introduce our research project to the Health Professionals Community and provide information on the traditional/cultural uses of North American ginseng, cutting-edge research on the effects of ginseng on health and future research directions. Additionally, our survey "Health Care Providers' Perspectives on Standards of Evidence in TCM and Ginseng Use" was introduced for comment and future participation. The OGIRC was a participant in the "Functional Foods & Natural Health Products: Staying Ahead of the Curve" Health Professionals' Day with more than 100 dietitians, naturopaths and other health professionals. In addition, OGIRC partners the Ontario Ginseng Growers Association contributed ginseng tea to the Functional Foods Lunch. Dr. Lui also gave a 30-minute presentation on the popular Be Healthy Stage entitled "What every health care provider should know about ginseng the miracle herb!"

5. *Pre-Clinical Workshop*

December 1, 2010

The objective of this workshop, "Moving from pre-clinical research to clinical trials" was to prepare and formulate clinical (and basic) research projects to extend the current OGIRC funded preclinical studies. Presentations were made by individual members of the pre-clinical group to summarize their research and key findings. Invited experts included Drs. David Spence, J. Malcolm Arnold and Jawaid Younus who shared their experience in clinical studies with the group. In addition, Dr. Suma Ramagiri, an application scientist with AB SCIEX provided an overview of their mass spectrometry system and its use in metabolic.

6. *Advanced Processing Workshop*

March 10, 2011

This workshop was held to facilitate the planning of an "exit-point" for the entire project with creation of new, value-added Ontario ginseng products proven to be effective and safe. The workshop encouraged collaboration among all the platform technology groups particularly Pre-clinical and Advanced Processing. Members of the OGIRC Advisory Committee were also in attendance to further their understanding of advanced processing and offer feedback on how the research could lead to potential commercial applications.

7. Journal Club

The OGIRC continued to hold Journal Club meetings in Year 3 to provide trainees with an opportunity to present their research proposals or findings, and to introduce consortium members to their research interests, thereby enhancing the inter-disciplinary experience.

Date	Presenter (Supervisor, PTG)	Title
Oct 2010	Yan Wu (Qingping Feng, Pre-clinical)	Ginseng protects the heart from ischemia-reperfusion injury via P13K/Akt/eNOS pathway
	Robert Bi (Jesse Zhu, Advanced Processing)	Value-added Ontario ginseng products
Dec 2010	Subhrojit Sen (Subrata Chakrabarti, Pre-Clinical)	American Ginseng Prevents Extracellular Matrix Formation in Diabetic Nephropathy
Jan 2011	Melissa Moey (Morris Karmazyn, Pre-clinical)	Ginseng attenuates leptin-induced cardiac hypertrophy through inhibition of the RohA/ROCK and associated pathways
	Megan Migchels (John Ciriello, Pre-clinical)	Chronic North American ginseng administration alters metabolic variables in the rat
Feb 2011	Colin Carruthers (Kem Rogers, Pre-Clinical)	Influence of North American ginseng extract on the initiation and progression of atherosclerosis
	Mao Jiang (Earl Noble, Pre-clinical)	American ginseng acutely regulates contractile function of the heart
Mar 2011	Mehrnaz Salarian (Paul Charpentier, Advanced Processing, Phytochemistry)	An injectible angiogenic poly(propylene fumarate)/TiO ₂ based bone cement
	Raziye Samimi (Paul Charpentier, Advanced Processing, Phytochemistry)	Extraction of ginsenosides from NA ginseng: selectivity and immunoactivity

8. Jamieson Graduate Student Travel Award

This generous support of graduate student research was announced in Year 3. Travel funds will be made available in Year 4 to defray expenses incurred by graduate students to present their ginseng research at a significant national conference (up to \$700) or international conference (up to \$1,400).

9. Media Articles

The OGIRC received favourable press in Year 3:

- Today Daily News, “OGIRC-CICMR Conference”, October 31 2010
- Royal Agricultural Winter Fair presentation on Health Professionals’ Day by Ed Lui, Ontario Ginseng Innovation & Research Consortium: “What every health care provider should know about ginseng the miracle herb!”, November 10, 2010.

<http://royalfair.org/HealthVideos>

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- Greenhouse Canada, “East Meets West: Guelph researcher uses controlled greenhouse environments to mass-produce medicinal plants”, December 2010
- Toronto Star, “The power of ginseng”, December 31 2010
- Research@Western, “Ed Lui: East meets Western”, January 2011

IV. OGIRC Governance

Management Committee

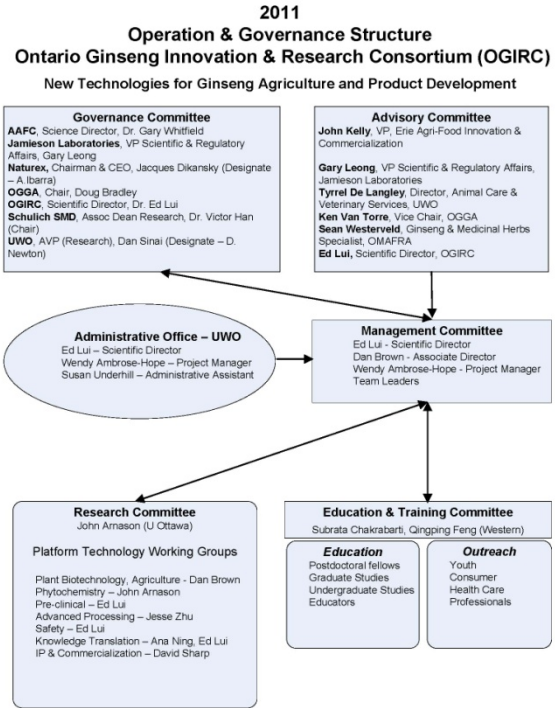
The Management Committee is comprised of the Project Manager, Scientific Director, Associate Director and the Platform Technology Group leaders. The Management Committee’s mandate is to oversee the scientific progress of the OGIRC and ensure all Milestones and Deliverables committed to in the ORF Grant Agreement are met.

The Management Committee met in June 2010 to discuss items such as research progress and milestones; encouraging and broadening the multi-disciplinary focus of the trainees; outreach and conference events; and methods to improve the collection of information from the members for inclusion in the ORF Annual Progress Report.

Governance Committee

The OGIRC Governance Committee’s objective is “To provide forward-thinking leadership and guidance, feedback and strategic planning to ensure the performance and fiduciary responsibilities of the Project are met”; and is responsible for providing vision and recommendations for future administrative and managerial actions, providing fiduciary oversight and reviewing and endorsing the Annual ORF Progress report prior to its submission. The committee membership is based on organizational position, and is comprised of representatives from AAFC (Science Director), Jamieson Laboratories (VP Scientific & Regulatory Affairs), Naturex (Chairman/CEO or Scientific Manager), the Ontario Ginseng Growers Association (Chairperson), Schulich School of Medicine & Dentistry (Dean or Associate Dean of Research), and the University of Western Ontario (Vice President – Research & International Relations, or Associate Vice President – Research).

The Governance Committee met on May 10, 2011, prior to the submission of the Year 3 ORF report to the Ontario Ministry of Research & Innovation. At this meeting, a motion to pass the ORF Annual Progress Report to the Ontario Ministry of Research & Innovation was passed unanimously. Challenges and opportunities for Year 3 and beyond in the areas of training, communications, IP and administrative issues were discussed. It was suggested that the Platform Technology Group leaders be invited to the next Advisory Committee meeting. The Governance Committee suggested that selected medicinal effects be focused on in years four and five and resources should be directed to activities that will fulfill the objective and deliverables of the Ontario Research Fund grant. The committee commented that as OGIRC continues to make steady progress on its HQP recruitment, research milestones and deliverables, and financial/administrative management.



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Advisory Committee

The Advisory Committee was established with with an objective of using the diverse experience and expertise of its membership to advise on the overall direction of the multi-disciplinary OGIRC to provide guidance in the identification of potential collaborations; funding opportunities; new direcitons for research; Intellectual Property (IP) issues; commercialization and market strategies. The committee is comprised of representatives with an interest and background in the ginseng and Natural Health Product sector.

The committee met in October 2010 for an introductory meeting for an introduction to the OGIRC and overview of its progress to date. A round-table discussion followed to discuss future initiatives. The committee met again March 2011 with an invitation to the Advance Processing Workshop to further their knowledge on the facilities and capabilities available within this technology platform group followed by a closed committee meeting. The committee expressed a positive view on both the quantitative and qualitative aspects of the OGIRC accomplishments and has provided suggestions and recommendations for securing additional support and resources; advice on potential directions for commercialization of ginseng products, including brand and certifications on Ontario ginseng.

V. Sponsorship

The Ontario Ginseng Innovation & Research Consortium (OGIRC) acknowledges the following sponsors and partners:

Government Sponsors

- The Ontario Ministry of Research & Innovation
- Agriculture and Agri-Food Canada

Private Sector Sponsors

- Naturex Inc.
- Jamieson Laboratories Inc.
- A&L Laboratories Inc.
- Ontario Ginseng Growers Association

Institutional Partners

- The University of Western Ontario
 - Schulich School of Medicine & Dentistry
- The University of Guelph
- McMaster University
- University of Ottawa
- Northern Ontario School of Medicine

VI. OGIRC Membership

Researchers (April 2010 – March 2011)

Plant Biotechnology PTG

Dan Brown (AAFC)
Praveen Saxena (U Guelph)

Advanced Processing PTG

Jesse Zhu (UWO)
John Arnason (U Ottawa)
Paul Charpentier (UWO)

Knowledge Translation PTG

Ana Ning (King's College)
Ed Lui (UWO)

Phytochemistry PTG

John Arnason
Paul Charpentier

Safety PTG

Ed Lui (UWO)
David Bailey (UWO)
Valter Feyles (UWO)
Andrew Watson* (UWO)

Commercialization & IP PTG

David Sharp (UWO)

Pre-Clinical PTG

Marica Bakovic (U Guelph)
Subrata Chakrabarti (UWO)
John Ciriello* (UWO)
Lique Coolen (UWO)
Qingping Feng (UWO)
Jim Henry (McMaster)
Morris Karmazyn (UWO)
Ed Lui (UWO)
Joachim Madrenas (UWO)
David Mutch* (Guelph)
Earl Noble (UWO)
Kem Rogers (UWO)
Zach Suntres (NOSM)
John Trevithick (UWO)

*Associate Member

OGIRC Trainees (April 2010 – March 2011)

Plant Biotechnology PTG

VS Binhu (PDF)
Mukund Shukla
Esther Uchendu (PDF)
Di Wu (PDF)
Sijun Zhou (PDF)

Phytochemistry PTG

Chike Azike (GS)*
Jose Guerrero (PDF)

Pre-Clinical PTG

Misagh Alipour (GS)
Chike Azike (GS)*
Matthew Barnes (GS)
Colin Carruthers (GS)
Luan Chau (T)
Jessica Davie (T)
Tomasz Dzialosynski (T)
Mehrbod Estaki (GS)
Juan Guo (PDF)
Jirui Hou (PDF)
Mao Jiang (PDF)
Holly Lemmon (GS)

Advanced Processing PTG

Kazi Akhter (GS)
Robert Bi (PDF)
Ying Ma (T)
Mehrnaz Salarian
Raziye Samimihaghgozar

Safety PTG

Danyka Belanger (GS)
Cheryl Lui (UGS)

Cheryl Lui (UGS)
Megan Migchels (GS)
Hoda Moazzen (GS)
Melissa Moey (GS)
Hua Pei (T)
Subhrojit Sen (PDF)
Ratnesh Singh (PDF)
Yufang Wang (PDF)
Sarah Wilson (UGS)
Yan Wu (GS)
Ganjian Zhao (PDF)
Yong Fang Zhu (PDF)

GS = Graduate Student
PDF = Postdoctoral Fellow
UGS = Undergraduate Student

MS = Medical Student
T = Technician

*co-supervised by members of different PTGs

Trainee Recognition & Awards

- *Cheryl Lui (Bailey-Undergraduate Co-op Student)* Poster presentation award, OGIRC/CICMR 2nd Joint Conference.
- *Melissa Moey (Karmazyn-MSc student)* Poster presentation award, 2nd place, J.A.F. Stevenson Research Day.
- *Melissa Moey (Karmazyn-MSc student)* Oral presentation award, OGIRC/CICMR 2nd Joint Conference.
- *Ratnesh Singh (Bakovic – PDF)* CGCM Travel Grant (9th CGCM Meeting, Hong Kong, August 2010).
- *Ester Uchenda (Saxena – PDF)* Poster presentation award, OGIRC/CICMR 2nd Joint Conference.
- *Lin Zhu (Bakovic – PDF)* Postdoctoral poster award, Canadian Lipoprotein Conference.

VII. New Funding Applications and Networking Activities

The OGIRC sought out new collaborators and funding sources in Year 3:

- NSERC CREATE – “Innovative Technologies for Agriculture and Medicinal Plant Product Development”. PI: EMK Lui with Co-I’s: D Brown, JT Arnason
- Ontario Ministry of Agriculture, Food & Rural Affairs (OMAFRA) – New Directions Research Program “Evidence-based value-chain model and marketing strategy for novel red Ontario-grown North American (NA) ginseng products”

PI: EMK Lui

The objective is to diversify and expand Ontario ginseng agriculture and production by transforming a cultural product into highly-valued, evidence-based red ginseng materials suitable for commercialization to serve local and international markets.

International Partners	National Partners
<ul style="list-style-type: none"> • Jeffrey Yeung (Hang Fat Ginseng Ltd) • Albert Wong (Zigen Pharmaceuticals) 	<ul style="list-style-type: none"> • Dan Brown (Agriculture and Agri-Food Canada) • Paul Charpentier (Chemical & Biochemical Engineering, UWO) • Key Lee (Canada Ginseng Technology Inc.) • Mario Slegers (MP Slegers Ltd) • Robert Ellis (AB SCIEX)

- Ontario Ministry of Tourism & Culture – Convention Development Fund (in partnership with Tourism London) “Natural Bioactives Conference 2012” (\$36,000)

VIII. Publications & Presentations:

Publications

In Year 3, the following articles were published by OGIRC members on their ginseng research:

- **Deschambault B., M. Bakovic, and D. Mutch** 2010. Nutritional genomics in obesity prevention and treatment. In: Obesity Prevention-A handbook for Integrative Science, Policy and Action to Stop the Progression of the Obesity Pandemic (Eds: Laurette Dube et al.), Chapter 30: 375-390
- **Guo J, Gan XT, Rajapurohitam V, Zeidan A, Faruq NS, Karmazyn M.** Ginseng inhibits cardiomyocyte hypertrophy and heart Failure via NHE-1 inhibition and attenuation of calcineurin activation. *Circulation: Heart Failure* 4:79-88, 2011
- **Wu Q, Henry JL.** Changes in A δ non-nociceptive primary sensory neurons in a rat model of osteoarthritis pain. *Molecular Pain* 6:37; PMID 20594346, 2010.
- **Chao Sun, Ying Li, Qiong Wu, Hongmei Luo, Yongzhen Sun, Jingyuan Song, Edmund M.K. Lui and Shilin Chen.** 2010. De novo sequencing and analysis of the American ginseng root transcriptome using a GS FLX Titanium platform to discover putative genes involved in ginsenoside biosynthesis. *BMC Genomics*, 11:262. <http://www.biomedcentral.com/1471-2164/11/262> (2 citations)
- **Mele T & Madrenas J.** 2010. TLR2 signalling: At the crossroads of commensalism, invasive infections and toxic shock syndrome by *Staphylococcus aureus*. *International Journal of Biochemistry and Cell Biology*. 42 (7): 1066-1071.

- **McIntyre K**, Liu A, Sun C, **Brown D**, **Lui EMK** and **Arnason JT**. Ginsenoside Variation Within and Between Ontario Ginseng Landraces: Relating Phytochemistry to Biological Activity. *Rec. Advances in Phytochem.* 41: 97-107 2011.
- Luu A, Foster B, **McIntyre K**, Tam T, and **Arnason JT**. Pharmacogenetics in Potential Herb–Drug Interactions: Effects of Ginseng on CYP3A4 and CYP2C9 Allelic Variants. *Rec. Advances in Phytochem.* 41: 59-66. 2011.

Submitted Manuscripts

The following manuscripts had been submitted for publication by the end of Year 3:

- **Azike C**, **Lui EMK**, **Charpentier P**, **Hou, J**, **Pei, H**. The Yin and Yang Actions of North American Ginseng Root in Modulating the Immune Function of Macrophages. *Chinese Medicine Journal*, 2011
- Dableh LJ, **Henry JL**. Neuropathic pain as a process: reversal of chronification in an animal model. *J Pain Research*, 2011
- Wu Q, **Henry JL**. Functional changes in muscle spindle afferent neurones in an osteoarthritis model: implications for impaired proprioceptive performance.
- **Moey M**, Rajapurohitam V, Zeidan A and **Karmazyn M**. Ginseng (*Panax quinquefolius*) attenuates leptin-induced ventricular cardiac hypertrophy through inhibition of p115RhoGEF-RhoA/ROCK-dependent MAPK pathway activation. Submitted to the *Journal of Pharmacology and Experimental Therapeutics (JPET)*.
- **Sen S**, Chen S, Feng B, Wu Y, **Lui EMK**, **Chakrabarti S**. American Ginseng (*Panax Quinquefolius*) Prevents Glucose-Induced Oxidative Stress And Associated Endothelial Abnormalities. *Phytomedicine*
- **Suntres Z.**, **Alipour M.**, **Omri A**. Ginseng aqueous extract attenuates the production of virulence factors, stimulates twitching and adhesion, and eradicates biofilms of *Pseudomonas aeruginosa*. Submitted to the *Canadian Journal of Physiology and Pharmacology* (Manuscript number: 2011-0090).
- **Uchendu, E.E.; Brown, D.C.W. and Saxena P.K.** 2010. Cryopreservation of Shoot Tips and Cotyledons of The North American Ginseng (*Panax quinquefolius* L.). *CRYOLETTERS*.
- **Uchendu, E.E.; Paliyath, G.; Brown, D.C.W. and Saxena, P.K.** 2011. In vitro propagation of North American ginseng (*Panax quinquefolius* L.). *In Vitro Cellular and Developmental Biology-Plants*.
- **Uchendu, E.E., Shukla, M.R.,** Reed, B.M., **Brown, D.C.W** and **Saxena P.K.** 2010. Improvement of Ginseng by In Vitro Culture: Challenges and Opportunities. *COMPREHENSIVE BIOTECHNOLOGY*, Murray Moo-Young (ed) 2nd edition, Elsevier. The Netherlands.
- **Wu Y**, Lu X, Xiang FL, **Lui EMK**, **Feng Q**. Ginseng protects the heart from ischemia and reperfusion injury via upregulation of endothelial nitric oxide synthase. *Pharmacological Research*.
- **Zhu Y**, Wu Q, **Henry JL**. Changes in functional properties of A-type but not C-type sensory neurons in vivo in a rat model of peripheral neuropathy.

Presentations

OGIRC members and HQP have attended national and international conferences to present their ginseng research

1. Azike C, Hou J, Pei H and Lui EMK. The modulation of polysaccharide extracts of North American Ginseng root on macrophages. 3rd Annual Cancer Drug Discovery Symposium, May 28 – 29, 2010, Sudbury ON. (contributed poster)

2. Bakovic M and Duric M. University of Guelph Food for Health. 9th meeting of the Consortium for Globalization of Chinese Medicine-Hong Kong, [August](#), 2010 (contributed poster).
3. Bakovic M. The Membrane Phospholipid Gene Pcyt2 Functions as a Barrier to Metabolic Disorders CMBD Seminar Speaker University of New Mexico HSC, December 10, 2010
4. Barnes M and Coolen L. Effects of North American Ginseng on Sexual Behaviour and Erectile Function in Healthy Rats. Society for Behavioural Neuroendocrinology 14th Annual Meeting. July 18 – 21, 2010. Toronto, ON. (contributed poster)
5. Brown, D.C.W., Zhou, S., Bhinu, V-S, Arnason, J.T. and McIntyre, K.L. 2010. The development and characterization of North American Ginseng (*Panax quinquefolius* L.) Germplasm. 10th International Symposium on Ginseng. Sept 13 – 16, 2010. Seoul, Korea (contributed poster)
6. Carruthers C, Davie J and Rogers K. North American Ginseng reduces expression of vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 *in vitro*. 10th International Symposium on Ginseng. Sept 13 – 16, 2010. Seoul, Korea (contributed poster)
7. Chakrabarti S, Sen S, Chen S, Feng B, Lui EMK. *Panax quinquefolius* (American ginseng) prevents chronic complications in Type 1 & Type 2 diabetes through its antioxidative and antihyperglycemic effects. 10th International Symposium on Ginseng. Sept 13 – 16, 2010. Seoul, Korea (contributed poster).
8. de Vrijer B, S Kim-Fine, J Fairbairn, J Greenspoon, SA Folliott, EMK Lui, TRH Regnault. The Influence of Fetal Gender, *Coriolus Versicolor* or *Panax Quinquefolius* on the Placental and Fetal Immune Response. Fetal and Neonatal Physiological Society Conference 2010, Winchester UK, July 4 - 7 2010.
9. Guo J, Gan XT, Rajapurohitam V, Zeidan A, Faruq NS, Karmazyn M. Ginseng inhibits cardiomyocyte hypertrophy and heart Failure *via* NHE-1 inhibition and attenuation of calcineurin activation. World Congress of the International Society for Heart Research, Kyoto, Japan, May 2010
10. Iqbal W, Moreau JM, Migchels MJ, Messenger SA, Ciriello J. Peripheral chemoreceptor excitation activates brainstem nesfatin-1-expressing neurons. Proc. of the Ontario Hypertension Society Annual Spring Conference, No. P2-17, 2010. Ontario Hypertension Society Annual Spring Conference, Alliston, ON; May 28 – 30, 2010. (contributed poster)
11. Lui EMK, Azike C, Zigler Z, Jirui H and Hua P. The Yin and Yang actions of NA ginseng roots in modulating the immune function of macrophages. 9th meeting of the Consortium for Globalization of Chinese Medicine, Hong Kong, Aug 23-25, 2010.
12. Lui EMK, Azike C, Hou J and Pei H. The Yin and Yang action of North American ginseng root in modulating the immune function of macrophages 10th International Symposium on Ginseng. Sept 13 – 16, 2010. Seoul, Korea (contributed poster)
13. Madrenas J. Immunology 2010 Baltimore: 97th Annual Meeting of the American Association of Immunologists. May 7 – 11, 2010, Baltimore Convention Centre (Presentation title not available).
14. Moey M, Rajapurohitam V, Zeidan A and Karmazyn M. Ginseng (*Panax quinquefolius*) attenuates leptin-induced ventricular cardiac hypertrophy through inhibition of p115RhoGEF-RhoA/ROCK-dependent MAPK pathway activation. 10 year Canada Research Chair Anniversary, Toronto ON, Nov 2010.
15. Saxena, PK (2010) Introducing novel herbal products in Canada: safety, quality and efficacy. 9th Meeting of Consortium for Globalization of Chinese Medicine (CGCM), Hong Kong, August 23 - 25, 2010 (contributed poster)
16. Sen S, Wu Y, Chen S, Feng B, McArthur K, Chakrabarti S. American Ginseng (*Panax quinquefolius*) prevents diabetes induced retinal changes. 9th Meeting of the Consortium of Globalization of Chinese Medicine. Hong Kong, Aug 23-24 2010 (contributed poster).
17. Singh RK, Duric M and Bakovic M. Ginseng Effects on Intestinal Lipid Secretion and Plasma Clearance in *Pcyt2*-Deficient Mouse Model for Metabolic Syndrome. 9th meeting of the Consortium for Globalization of Chinese Medicine. Hong Kong, [August](#), 2010

18. Trevithick J, Dzialoszynski T and Noble E. Modeling space radiation cataract risk reduction by Antioxidants and Ontario Ginseng Extract. Poster presentation at ARVO 2010, Fort Lauderdale FL, May 2 – 6, 2010.
19. Trevithick J, Dzialoszynski T and Noble E. High energy proton and neutron astronaut model cataract risk reduction by antioxidants and Ontario ginseng. ASTRO 2010, Toronto ON, May 4 – 6, 2010. (Contributed talk).
20. Wu, D. **Zhou, S.** Brown, D.C.W. 2011. Transcriptome sequencing of North American Ginseng using the 454 GS FLX Titanium platform. OGGA Annual General Meeting, Delhi, March 29 2011 (contributed poster)
21. Wu Y, Lu X, Xiang FL, Feng Q. Ginseng protects the heart from ischemia and reperfusion injury by activating PI3K/Akt-dependent eNOS pathway. Poster presentation at World Congress of the International Society of Heart Research, Kyoto, Japan, May 13-16, 2010.
22. **Zhou, S.** and Brown, D.C.W. 2010. An efficient protocol for micropropagation of North American ginseng. Abstract Book, 12th IAPB Congress, St. Louis, Missouri, USA, June 6-11 2010 (contributed poster)
23. **Zhou, S.** and Brown, D.C.W. 2011. Micropropagation of North American ginseng. OGGA Annual General Meeting, Delhi, March 29 2011 (contributed poster)

Technical Reports

Lui, EMK (2011). Annual report of the OGIRC to the Ontario Ginseng Growers Association.

IX. Administration and Financial Management – April 2010 to March 2011

The OGIRC central office continued in Year 3 to manage the regulatory and administrative details of the ORF grant and act as a central point of contact and communication for the consortium members.

Staffing

The central office continued to be staffed by full time project manager, Wendy Ambrose-Hope and part-time administrative assistant, Jennifer Heidenheim. Over the course of the year the Work Study program was utilized to supplement staffing needs, particularly for planned events and production of exhibit material. Interdisciplinary opportunities were also provided to out of faculty students who had little experience with the research enterprise at Western.

Activities

The office coordinated and supported a number of activities throughout the year including: three grant submissions, a summer retreat, the administration of the OGIRC/CICMR Joint Conference at University of Ottawa, as well as the group travel arrangements for the membership to attend, preparation of outreach material for the weeklong exhibit at 2010 Royal Agricultural Winter Fair. A funding submission to Tourism London secured \$36,000 cash and in-kind support for a significant international conference to be held summer 2012. The office coordinated and supported six Journal Club meetings, two research workshops (Pre Clinical and Advanced Processing) and two Advisory Committee meetings.

General Administration

On a quarterly basis, the office monitors the expenses of *all* investigators that have received funds from the home grant and collects records of matching “in-kind” contributions from the OGIRC membership including partner organizations. In addition, an annual progress report is prepared by the office and facilitated by the collection of reports from every trainee, investigator and group leader. The data collected from 45 individual reports is reviewed, notated and compiled into a comprehensive report to the Governance Committee and the province in the form of the ORF Report. Records are also kept of the members’ activities in regard to HQP recruitment, publications, research reports and travel for the ongoing management of the project

Initiatives for Year 4

A number of initiatives have been identified for the upcoming year:

- Exhibit at Discovery 2011 an Ontario Centres of Excellence event
- Initiate conference planning for international conference in summer of 2012
- Facilitate site visit to Jamieson Labs
- Participate in the Indigenous Youth Summer Camp offered by Western’s Indigenous Services, a camp to inspire indigenous youth to attend university.
- Enhance admin database to include publications and activities and training participation
- Enhance website to include publication citations
- Establish presence on a social media site (Facebook)

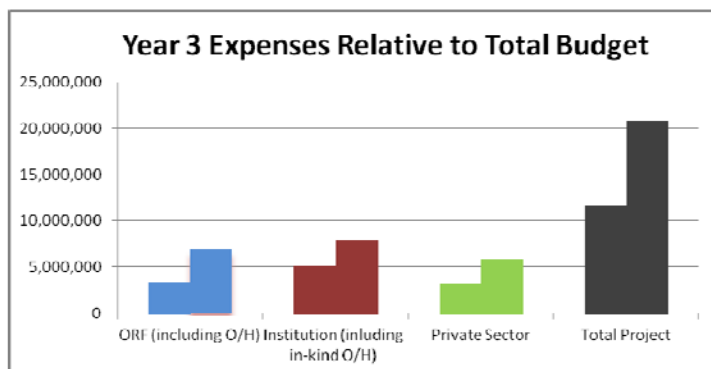
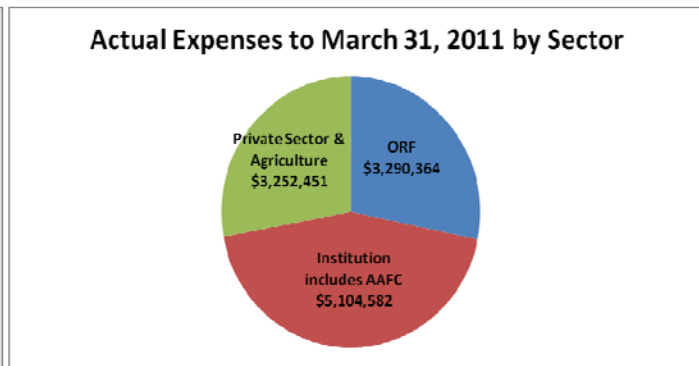
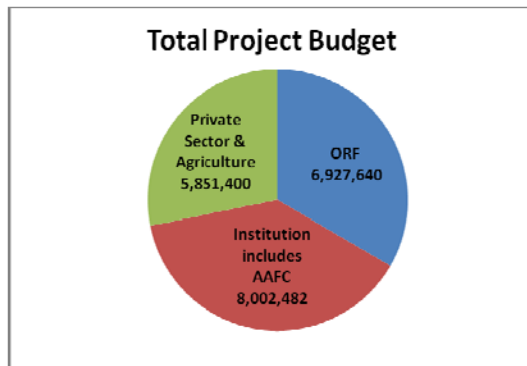
Ontario Ginseng Innovation & Research Consortium Financial Report April 1, 2010 to March 31, 2011

Cash/In Kind Expenses Reported in Year 3

April 1, 2010 to March 31, 2011

	ORF	Institution	Industry		Total
			Cash	In Kind	
PI Salaries & Benefits		456,637	-	-	456,637
Personnel Salaries & Benefits	604,185	262,920	-	335,757	1,202,862
Facilities	-	-	-	-	-
Equipment	-	-	-	-	-
Research Expenses	324,801	217,082	-	610,453	1,152,336
Conference	-	7,458	14,108	-	21,566
Travel/Visitors	29,462	-	-	3,100	32,562
Mgmt & Admin - S&B	122,629	-	-	14,030	136,659
Mgmt & Admin - Other	667	-	-	-	667
Youth Outreach	-	-	-	-	-
Audit	11,287	-	-	-	11,287
Total Cash Expenses	1,093,031	944,097	14,108	963,340	3,014,576
Total Overhead (Cash/In Kind)	437,212	768,618	-	-	1,205,830
Total Cash/In Kind Expenses	1,530,243	1,712,715	14,108	963,340	4,220,406

*Institution makes in kind contribution by not assessing overhead on Industry \$'s



Note: Auditors' Report dated September 21, 2011 for Year ended March 31, 2011 available