Cl**n**cal Research Office **
Shared Resource**

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**Shared Resource Code:** CRO

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**OVERVIEW**

The Clinical Research Office (CRO) coordinates the activities and provides oversight for clinical research studies conducted by Cancer Center Members. The CRO is located in the 4th floor of the Cancer Center and it is formed by the Therapeutics Research Office (TRO), the Prevention Research Office (PRO) and the Recruitment Office (RO) and it works in a very close collaboration with the Regulatory Affairs Office (RAO) and the Informatics services. Specifically, the objectives of the Shared Resource are to:

- Facilitate protocol activation and give protocol support to cancer related research studies
- Facilitate protocol management and conduct of therapeutic, prevention and intervention trials
- Promote awareness and facilitate dissemination of information of active clinical trials to cancer center health care providers and investigators
- Facilitate screening/enrollment of potential candidates onto clinical trials
- Provide central informatics services and accurate reporting for CC clinical research protocols
- Generate an adequate protocol portfolio targeting the existing patient population and prioritizing by protocol type (investigator initiated, clinical trials to cancer center health care providers and investigators
- Research studies
- Perform quality assurance, research compliance and adherence to GCP
- Through internal or external auditing and monitoring as appropriate)
- Comply with mandatory protocol listing/reporting to the general public

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**RESEARCH SUPPORTED**

**UCI 07-61 Phase II Study of Breast Cancer Treatment Using Weekly Carboplatin + Nab- paclitaxel, Plus Trastuzumab (HER2+) or Bevacizumab (HER2-) in the Neoadjuvant Setting:** Su (OIS), Mehta (OIS), Butler (OIS), Hsiang (OIS), Bahri.

This NCI supported Investigator Initiated study with 54 treated subjects and 25% of them have had pCR to treatment. This study is designed to estimate 2 year progression-free survival in patients with more than 1 cm and/or lymph node positive breast cancer treated with weekly Carboplatin/Nab-Paclitaxel(with trastuzumab in patients with HER2+ disease, and with bevacizumab in HER2-) when treated in the neoadjuvant setting. The study has a very important imaging component designed to find a reliable monitoring method, the Dynamic Contrast Enhance MRI (DCE-MRI), to obtain pre-treatment tumor characteristic morphological, enhancement kinetic, and Choline metabolic parameters in breast cancer, through selection of an optimal set of features using the logistic regression analysis and the Artificial Neural Network (ANN) to predict pathologic complete remission (pCR) in HER-2 positive and negative arms. MRI evaluation results were presented in the Radiological Society of North America in Chicago, on 11/28/10 and at the San Antonio Breast Cancer symposium on 12/8/10.

Example of accurate DCE-MRI diagnostic to positive treatment response (PR-1819087)

**UCI 06-60: A Phase II Trial of Dasatinib in Subjects with Hormone-Refractory Prostate Cancer Previouly Treated with Chemotherapy.**

This HDII trial examined the response rate and multiple biochemical parameters in subjects treated for hormone-refractory prostate cancer with dasatinib, a multi-targeted kinase inhibitor. 38 patients were enrolled and 27 were eligible and treated. Four subjects had evidence of a positive effect (CR, PR, or SD) which at times were dramatic, while the remainder had progressive disease or discontinued treatment due to toxicity. The correlative laboratory studies generated several hypotheses that suggest ways to improve the therapeutic effects of dasatinib. Of the 21 patients in whom paired (before/after) plasma samples were available, 8 had a 50% or greater decrease in IL6 level during the first 28 days of therapy (Fig. 4). All of the patients with positive effect were in this group, giving a response rate of 50%. No responses were seen among the 13 subjects with stable or increasing IL6. We have now seen that dasatinib itself can increase the level of IL6 in whole blood cultures (Fig. 5). These data suggest that the addition of an agent to block IL6 secretion may improve the therapeutic effect of dasatinib.

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**SERVICES PROVIDED**

- Initial protocol committee and IIR submission for protocol approval
- Participation in all relevant committees for accurate and efficient protocol development and/or compliance with GCP
- Communication with investigators for recruitment plans
- Development of additional subject recruitment tools and strategies
- Monthly publication of open accrual protocol flip book
- Accurate and opportune publication of approved documents for clinical research
- Support at all levels of protocol conduct:
  1. Informed consent process
  2. Eligibility verification
  3. Registration and randomization
  4. Coordination of all required interventions during subject intervention (either therapeutic, prevention or intervention trials) including pharmacy accountability and nursing coordination
  5. Reporting of clinical outcome and toxicity, and accurate data recording, gathering and reporting
  6. Internal and external monitoring as applicable
  7. Maintenance of research subject confidentiality
  8. Internal/external reporting for CSG compliance or internal strategic planning

Further information regarding all offered services can be found at our Web site: http://www.cancer.uci.edu/resources/clinical_research_office.html

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**ACHIEVEMENTS**

- 18 Cancer Publications
- 39 Cancer Sponsored Projects
- 21 Unique Cancer Center Users
- 4% CCSG Income / 75% of Use by Cancer Center Members

**CAPACITY OF RESOURCE USED**100%

<table>
<thead>
<tr>
<th>Name of Service</th>
<th>Unit of Measure</th>
<th>Definition of Unit of Measure</th>
<th>Total Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory Affairs Office, Initial Protocol Support</td>
<td>Hours</td>
<td>Hours of work</td>
<td>10,112</td>
</tr>
<tr>
<td>Protocol Implementation &amp; Management</td>
<td>Hours</td>
<td>Hours of work</td>
<td>14,172</td>
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<tr>
<td>Data Management</td>
<td>Hours</td>
<td>Hours of work</td>
<td>9,302</td>
</tr>
<tr>
<td>Informatics Reporting &amp; Analysis</td>
<td>Hours</td>
<td>Hours of work</td>
<td>1,044</td>
</tr>
<tr>
<td>Recruitment Office, Screening &amp; Accrual Support Services</td>
<td>Hours</td>
<td>Hours of work</td>
<td>1,830</td>
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<tr>
<td>Total</td>
<td></td>
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<td>36,460</td>
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</table>

**NEW & FUTURE DEVELOPMENTS**

What is new:

- Excellent accrual and activity in Phase I trials particularly for UCI 07-40: Phase I Safety, Pharmacokinetic and Pharmacodynamic Study of PT-0341/066, a C-MET/IGF3R Selective Tyrosine Kinase Inhibitor, Administered Orally to Patients with Advanced Cancer or crizotinib study; which has had interesting positive results and national attention for which the office is currently preparing for the first FDI audit in history.
- Expanded use of the Clinical Trials Management System to facilitate patient registration, electronic committee setting and accurate/opportune reporting

**Future developments:**

- Continue to support Phase I trials particularly those originated from the Translational Working Groups (i.e UCI-10-11 A Phase II Study to Evaluate the Effects of Docetaxel Plus Lycopen in Castration-Resistant, Chemotherapy-Naive Prostate Cancer Patients). This study is investigator initiated trial which ideas originated in the Prostate Translational Working group as science collaboration.
- Continue to expand the use of the CTMS for calendar/budget applications

**VALUE ADDED**

The CRO shared resource provides services that facilitate all the stages of protocols written by investigators or available at our center to support different levels of cancer research (prevention/therapeutic/diagnostic/supportive care). The full set of services starts with initial protocol evaluation at the committee level; it is present at all stages of protocol implementation and ends up at the level of data gathering and analysis. The CRO in our Cancer Center is the only one in its nature, within the UCI Medical Center, that provides one stop set of services for this type of research.

**TOTAL OPERATING BUDGET IN DOLLARS**

<table>
<thead>
<tr>
<th>Income Source</th>
<th>Current Support</th>
<th>Current Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Center Support Grant</td>
<td>$52,848</td>
<td>4%</td>
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<tr>
<td>Charge Backs</td>
<td>$419,640</td>
<td>33%</td>
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<tr>
<td>Institutional Support</td>
<td>$370,018</td>
<td>29%</td>
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<tr>
<td>Other</td>
<td>$436,450</td>
<td>34%</td>
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<tr>
<td>Total</td>
<td>$1,278,956</td>
<td>100%</td>
</tr>
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</table>

**UTILIZATION USER TYPE BY FUNDING**

<table>
<thead>
<tr>
<th>Source</th>
<th>Members w/PR</th>
<th>Members w/o PR</th>
<th>Non-members</th>
<th>Last 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associate Members</td>
<td>3%</td>
<td>8%</td>
<td>13%</td>
<td>4%</td>
</tr>
<tr>
<td>Carcinogenesis</td>
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<tr>
<td>Chemical Structural Biology</td>
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<tr>
<td>Growth Factors &amp; Signaling</td>
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<tr>
<td>Systems &amp; Developmental Biology</td>
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<tr>
<td>Onco Imaging &amp; Spectroscopy</td>
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<tr>
<td>Population Sciences &amp; Prevention</td>
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**SUPPORT PERCENT OF TOTAL CORE EFFORT**

- 0% 5% 10% 15% 20% 25% 30% 35% 40% 45% 50% 55% 60% 65% 70% 75% 80% 85% 90% 95% 100%

**Fig 1. 07/09/08
2.8cm lesion, 4.8cm node**

**Fig 2. 08/06/08
1.1cm lesion, 3.3cm node**

**Fig 3. 10/01/08
No residual lesion, 2.3cm node**

**Fig 4. Response of PCa to dasatinib correlates with a decrease in IL6 plasma level**

**Fig 5. Dasatinib stimulates secretion of IL6 in whole blood cultures**