Investment in Early Translational Cancer Research, 2005–2007

A special report from the Canadian Cancer Research Alliance's survey of government and voluntary sector investment in cancer research

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Canadian Cancer Research Alliance • Alliance canadienne pour la recherche sur le cancer

CANADIAN PARTNERSHIP AGAINST CANCER
PARTENARIAT CANADIEN CONTRE LE CANCER

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For additional copies of this publication, please contact:

Canadian Cancer Research Alliance (CCRA)
1 University Avenue, Suite 300
Toronto, Ontario M5J 2P1 CANADA
Tel.: (416) 915-9222, ext. 5739
Fax: (416) 915-9224
Email: info@ccra-acrc.ca

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1. Introduction

> *Research translation encompasses all of the processes involved in developing promising basic laboratory and epidemiological discoveries into cancer-related drugs and biologics, medical devices, behavioral interventions, methodologies, and instruments, and making these readily available to all segments of the public with cancer and those at risk for cancer.*

From Suzanne H. Reuben, *Translating Research into Cancer Care: Delivering on the Promise*. Bethesda, MD. President's Cancer Panel, 2004–2005 Annual Report, U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, June 2005, ii.

1.1 REPORT PURPOSE & PLAN

The impetus for this report was a question from Dr. Victor Ling, founding scientific director of the Terry Fox Research Institute: was it possible to quantify the investment in translational research from data gathered as part of the Canadian Cancer Research Survey (CCRS)? Other research funders and, more formally, the Canadian Cancer Research Alliance (CCRA) in its strategic plan,[1] echoed this need for information on how much and what kinds of translational research was being undertaken in Canada. The primary system for coding the data within the CCRS was the Common Scientific Outline (CSO), which was not specifically designed to identify translational research. Another classification system would be required to generate relevant investment figures.

This report aims to quantify the investment in translational cancer research using the CCRS as its source. It utilizes a comprehensive framework of translational cancer research developed by the U.S. National Cancer Institute (NCI), described in the following section. The report provides baseline data, which will allow new investments in translational research to be tracked. Furthermore, it may help research funders to identify gaps and potential bottlenecks to translational research as well as prospective solutions that will improve the implementation of innovative findings from "benchtop to bedside."

1. The CCRA *Pan-Canadian Cancer Research Strategy* (CCRA, 2010) devotes four of its 24 action items for the 2010–2014 period to research translation.

1.2 CLASSIFYING TRANSLATIONAL RESEARCH

Between 2005 and 2007, the U.S. National Cancer Advisory Board, under the auspices of its Translational Research Working Group (TRWG), sought to evaluate the U.S. National Cancer Institute's investment in translational research and enhance the productivity of the translational research enterprise in the U.S. Very early in its evolution, the TRWG recognized the importance of a shared vocabulary to facilitate its work -- although translational research is a significant part of the cancer research effort, "translational research" has no single standard definition and viewpoints on its nature and bounds vary.

The TRWG supported the broad and inclusive perspective on translational research proposed in the 2004–2005 Annual Report of the President's Cancer Panel report[2] (see Figure 1.1.1). In this conceptualization, translational research is conceived of in four main stages that follow basic science discovery and end in adoption/diffusion. The TRWG decided to focus its work on the "early translation" portion of the research translation continuum: "the translational process that follows fundamental discovery and precedes definitive, late-stage trials."[3] This phase is marked on the diagram below.

FIGURE 1.1.1

THE RESEARCH TRANSLATION CONTINUUM [1]

Basic Science Discovery	Early Translation	Late Translation	Dissemination	Adoption
• Promising molecule or gene target • Candidate protein biomarker • Basic epidemiologic finding	• Partnerships and collaboration (academic, government, industry) • Intervention development • Phase I/II trials	• Phase III trials • Regulatory approval • Partnerships • Production/ commercialization • Phase IV trials – approval for additional uses • Payment mechanism(s) established to support adoption • Health services research to support dissemination and adoption	*(of new drug, assay, device, behavioral intervention, education materials, training)* • To community health providers • To patients and public	• Adoption of advance by providers, patients, public • Payment mechanism(s) in place to enable adoption • Data collection to support outcomes research, intervention refinement, health services, and other research, and to inform provider practices

[1] The continuum is not unidirectional. In addition to transforming discoveries arising from fundamental laboratory, clinical, or population-based research into new drugs, devices, or population interventions, findings from the clinic and population may loop back and inform new early translational research projects designed to refine or expand the application of an innovation.

From Suzanne H. Reuben, *Translating Research into Cancer Care: Delivering on the Promise*. Bethesda, MD. President's Cancer Panel, 2004–2005 Annual Report, U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, June 2005, Figure 1, ii.

2. The President's Cancer Panel, established by the 1971 National Cancer Act, is charged with monitoring and evaluating the National Cancer Program and reports at least annually to the president of the United States.
3. From E.T. Hawk et al., "The Translational Research Working Group development pathways: Introduction and overview," *Clinical Cancer Research* 14(18), 2008: 5666.

The TRWG group developed process diagrams for six pathways to clinical goals, outlining the steps required to advance discoveries (e.g., laboratory research, basic epidemiological and behavioural research, etc.) to early-phase clinical trials. This typology of early translational cancer research is the most comprehensive paradigm produced to date and is well described in the TRWG report *Transforming Translation: Harnessing Discovery for Patient and Public Benefit*, published in June 2007, and a series of seven articles published in the 2008 (Vol. 14, No. 18) issue of *Clinical Cancer Research*.

An overview of the typology is provided in Figure 1.1.2. The typology is described more fully in the following chapter. It consists of six modalities—diagnostics and treatments/interventions intended to characterize or change an individual's cancer-related status. Each modality has four developmental phases, with an overarching phase of supporting tools, so named because it supports the research in the other phases.[4] The TRWG framework was chosen for this report because it is the most comprehensive one published to date and allows for comparative benchmarking.

FIGURE 1.1.2

OVERVIEW OF THE TRANSLATIONAL RESEARCH WORKING GROUP (TRWG) DEVELOPMENTAL PATHWAYS TO CLINICAL GOALS

		MODALITY					
	DEVELOPMENTAL PHASE	RISK ASSESSMENT (RA) Research intended to characterize the cancer-related health status of an individual		INTERVENTIVE (INT) Research intended to change the cancer-related health status of an individual via prevention or treatment			
SUPPORTING TOOLS	1 - CREDENTIALING	I. Biospecimen-based	II. Image-based	I. Agents (Drugs & Biologics)	II. Immune Response Modifiers	III. Interventive Devices	IV. Lifestyle Alterations
	2 - CREATION OF MODALITY						
	3 PRECLINICAL DEVELOPMENT						
	4 CLINICAL TRIALS						

Adopted from E.T. Hawk et al. (2009). The Translational Research Working Group Developmental Pathways: Introduction and Overview. *Clinical Cancer Research,* 14(18), 5664–5671.

4. Early in the NCI's foundational work on this paradigm, a pilot project was conducted to apply the framework and identify the institute's overall effort in translational research. (For details, please consult the summary of this analysis available at http://www.cancer.gov/researchandfunding/trwg/portfolio-analysis.pdf.) The authors found that translational projects were distributed in varying degrees across NCI award-sponsoring offices, centers, and divisions and, likewise, across many different funding mechanisms. On the downside, they concluded that the inclusion criteria used for the pilot project likely overestimated the degree of translational research relevance.

1.3 TAILORING THE TYPOLOGY TO THE CANADIAN CONTEXT

In this report, the TRWG typology and inclusion criteria have been tailored to the Canadian cancer research environment. In Canada, funding for direct support (operating grants), salary support, and equipment/infrastructure support often comes from different funding organizations in contrast to the all-inclusive support provided by many funding mechanisms offered through the NCI. Furthermore, the level of detail on equipment/infrastructure projects within the CCRS is, in most cases, limited and does not permit classification in terms of the TRWG phases. To account for the investment in equipment/infrastructure, an additional category was constructed. (Details are provided in the next chapter.)

This report provides vital data never before made available on early translational cancer research funding in Canada. It is based on research projects funded by the organizations that participated in the CCRS. For ease of interpretation, and given a lack of differences in the distribution of the investment from year to year, the investment figures were averaged for the period 2005 to 2007. Findings are presented in different ways to provide a comprehensive picture of what and where translational research is taking place.

1.4 REPORT COVERAGE

This report represents the portion of early translational research conducted in academic environments in the form of cancer research projects funded by major peer-reviewed programs offered by governments and charitable organizations in Canada. The pharmaceutical and medical devices industries, academic/health care institutions with monies raised by local hospital foundations, and government agencies through intramural research programs also conduct early translational cancer research. Canadian researchers also receive funding from out-of-country sources to support early translational cancer research projects.

An estimate of the total investment in early translational research was calculated to give some context to the figures reported herein. The dearth of publicly available information from which to derive estimates complicated this exercise. The estimations suggest that this report represents approximately 33% to 41% of the total annual early translational cancer research investment in Canada during the 2005 to 2007 period (see Table 1.4.1).

TABLE 1.4.1

ESTIMATED ANNUAL INVESTMENT IN EARLY TRANSLATIONAL CANCER RESEARCH, MAJOR SOURCES

SOURCE	Investment (millions of dollars)	%	Estimate Quality
This report/Canadian Cancer Research Survey	102	33–41	Good
Pharmaceutical industry [1]	110–120	36–48	Fair
Medical devices industry [2]	20–40	7–16	Poor
Hospital foundations [3]	10–30	3–12	Poor
Other intramural government funding [4]	1–5	Less than 1–2	Poor
Funders outside Canada [5]	4–8	1–3	Fair
TOTAL	**247–305**	**100**	

[1] Annual figures (2005–2007) for R&D by research type (i.e., preclinical trial I, preclinical trial II, clinical trial phase I and clinical trial phase II) for pharmaceutical companies in Canada are available from the Patented Medicine Prices Review Board (PMPRB) (see http://www.pmprb-cepmb.gc.ca). Although only companies with sales of patented medicines in a given fiscal period are required to report R&D expenditure to PMPRB, the intramural R&D figures shown in the PMPRB reports are very similar to those reported by Statistics Canada for the "Pharmaceutical and Medicine" industry (see *Industrial Research and Development: Intentions*, Catalogue No. 88-202-X), data which are based on a separate survey sponsored by Health Canada. Using U.S. National Institutes of Health's ClinicalTrials.gov, the largest database of government and privately supported clinical trials conducted in more than 170 countries, various searches were conducted to obtain estimates of the proportion of phases I and II industry-funded trials that are relevant to cancer. These estimates were then applied to the R&D figures reported by PMPRB.

[2] The Medical Device Industry Survey 2000, a one-time survey conducted by Statistics Canada, found a total R&D expenditure in 2000 of $126M by the Canadian medical devices industry. This included the following sector-specific expenditures: $26.7M medical imaging/radio-therapy, $9.1M medical surgical, $15.2M other hospital equipment/medical electronic, $8.5M assistive devices, $3.3M diagnostics, and $5.4M implants. The level of investment for 2005 to 2007 is not known. More significantly, there are no sources of data from which to estimate the cancer relevance of this investment.

[3] This estimate was based on annual reports of the Princess Margaret Hospital Foundation, the single largest hospital foundation in Canada and a hospital with an exclusive focus on cancer, and adjusted by the proportion of translational research for Princess Margaret Hospital as captured in the CCRS and then increased by 30% to reflect other hospital foundation funding.

[4] Specific intramural research activities conducted by organizations such as the National Research Council of Canada are likely relevant, although no publicly available data sources exist to estimate the extent to which they are translational and specific to cancer.

[5] Publicly available data from the NCI and Congressionally Directed Medical Research Programs (U.S. Department of Defense) were used to identify early translational research project funding and clinical trials infrastructure support provided to researchers in Canada for years 2005–2007. This averaged approximately $4.1 per year. Data are lacking, however, on the amount of additional support the U.S. government gives to Canadian sites for clinical trials and the amount of research support provided to Canadian researchers by other charitable organizations outside of Canada.

2. Methodology

Key abbreviations used in this document are written out in full in Appendix A. Unless otherwise noted, subsequent references to translational research refer to the early translation phase of the research translation continuum.

2.1 PROJECT IDENTIFICATION

The data source for this study was the CCRS database. This database is composed of peer-reviewed cancer research projects funded by 37 organizations/programs within the federal government, provincial government, and voluntary sectors from January 1, 2005 to December 31, 2007. It includes organizations that fund only cancer research (e.g., Canadian Cancer Society) and organizations that fund all types of health research (e.g., Michael Smith Foundation for Health Research), general research, and technology (e.g., Canada Foundation for Innovation).

The database includes all research projects funded by cancer research organizations. Research projects funded by other health/general science research funders, however, are assessed for their cancer relevance. A project is included only if cancer is specifically mentioned in the available project descriptions (face validity), with research projects on tobacco being the one exception.[5]

All projects in the CCRS database are coded in terms of the CSO, cancer site (using the International Statistical Classification of Diseases and Related Health Problems, ICD-10), and type of funding mechanism (definitions can be found in the sidebar). The CSO is an international standard for classifying cancer research. It is grouped into

DEFINITIONS OF FUNDING MECHANISMS

Career awards: competitive awards that provide protected time for research on either a long- or short-term basis to outstanding researchers who have demonstrated high levels of productivity and research accomplishments. These awards are given to only a small percentage of all researchers. (They may also be called salary awards.) Research chairs and establishment grants, grants designed to facilitate the recruitment of outstanding researchers, are also included under this funding mechanism.

Equipment/infrastructure grants: competitive grants that cover, in part or in full, the costs of construction or major remodelling of new research facilities, and/or the purchase, housing, and installation of equipment, scientific collections, computer software, information databases, and communication linkages used primarily for conducting research.

Operating grants: competitive grants that support all the direct costs involved in conducting specific research projects performed by identified researchers. Operating grants typically cover salaries for laboratory staff and research assistants/associates/trainees, costs of research equipment and supplies, and other specific research-related expenses. Multi-component projects (program projects), feasibility grants, proof-of-principle grants, regional development grants, innovation grants, and knowledge translation grants are all included in this category.

Related support grants: competitive grants that support travel, workshops/symposia, and researcher time for proposal development/letters of intent. These grants involve small sums of money.

Trainee awards: competitive awards that recognize outstanding trainees and support them during their undergraduate, graduate, or post-graduate training. Trainees from Canada who are studying at institutions outside Canada may also be eligible for some types of trainee awards. Block training grants given to institutions that in turn distribute the monies to trainees through a competitive process are also included under this funding mechanism. These awards are in addition to trainee salaries covered in operating grants.

5. All tobacco projects funded by the organizations contributing to the CCRS are included in the database unless the research is focused solely on diseases other than cancer.

seven categories (1-Biology, 2-Etiology, 3-Prevention, 4-Early Detection, Diagnosis, and Prognosis, 5-Treatment, 6-Cancer Control, Survivorship, and Outcomes Research, and 7-Scientific Model Systems), which are rolled up from 38 codes. (Details about the CSO can be obtained at http://cancerportfolio.org/cso.jsp.) The number of CSO codes assigned to projects in the CCRS ranges from one to nine.

The database currently holds 7,203 projects. For the purposes of this study, projects coded entirely to the CSO category 1-Biology (n=2,828) were not considered because it was assumed that they were basic discovery projects and out of scope. The remaining 4,375 projects were reviewed and either excluded or included as part of the study sample.[6] Excluded projects focused on:

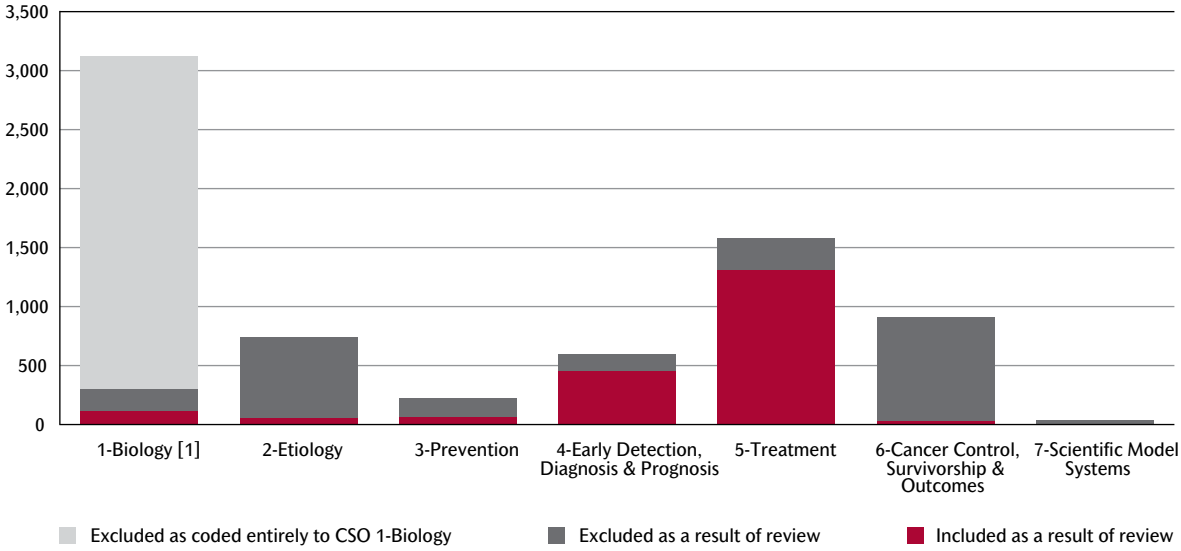
- basic discovery (biomolecular or epidemiological)
- model systems in which the research did not have immediate translational research goals
- surveillance, survivorship,[7] and outcomes research
- treatment of cancer-causing infectious diseases
- late translation (e.g., phase III clinical trials,[8] research on dissemination and/or adoption of a modality)
- provision of general/multi-faceted infrastructure
- training/capacity building and creation/maintenance of tumour banks/tissue repositories not directly linked to specific translational research activities/modalities. These projects are listed in Table 3.1.1 in the next chapter to recognize that these funded resources are essential for the conduct of translational research, although they are not translational research projects themselves.

The final sample consists of 2,043 projects. Figure 2.1.1 shows the composition of the final sample and excluded projects in terms of the CSO categories.

6. Projects coded to 1-Biology and another CSO code were included in the reviewed group of projects.
7. Investment in survivorship research will be the focus of an upcoming study by the CCRA.
8. Phase III clinical trials within the CCRS represented an investment of $2.5M per year.

FIGURE 2.1.1

PROJECTS EXCLUDED FROM AND INCLUDED IN THE FINAL SAMPLE BY COMMON SCIENTIFIC OUTLINE (CSO) CATEGORY



[1] Projects coded to 1-Biology and another CSO code were reviewed and in a small number of cases, included in the final sample.

To assess the reproducibility of the exclusion criteria, an independent coder reviewed a random sample of 400 projects of the previously mentioned remaining 4,375 projects. Observed agreement between the primary and secondary coders was 90.3% overall and ranged from 84.4% for projects coded in whole or in part to CSO category 4-Early Detection, Diagnosis & Prognosis to 100% for projects coded in whole or in part to CSO category 7-Scientific Model Systems. The Cohen's kappa coefficient (unweighted) was 0.81 (95% confidence intervals 0.75–0.86), indicating "almost perfect agreement," according to the interpretation guidelines developed by Landis and Koch.[9] For the sample of projects involved in the inter-rater reliability assessment, the two coders discussed discordant coding and they made a final inclusion/exclusion determination.

2.2 PROJECT CLASSIFICATION

This report incorporates the TRWG development pathways as its primary classification framework (as per Figure 1.1.2). The pathways typology distinguishes two classes of clinical modalities: risk assessment and interventive. **Risk assessment** modalities (RA) *characterize* the cancer-related health status of an individual and consist of biospecimens (biological molecules found in blood, other body fluids, or tissues) and Image-based devices (e.g., computed tomography, contrast agents, and imaging enhancers). **Interventive** modalities (INT) *change*

9. J.R. Landis and G.G. Koch, "The measurement of observer agreement for categorical data," *Biometrics* 33, 1977:159–174.

the cancer-related health status of an individual by either prevention or treatment and consist of Agents (drugs or biological compounds), Immune Response Modifiers (agents that mimic, augment, or require participation of a person's immune cells for optimal effectiveness), Interventive Devices (e.g., radiation therapy, cryoablation, high-intensity focused ultrasound), and Lifestyle Alterations (behavioural changes). The developmental process underlying all six pathways consists of four phases:

- **Credentialing**: research that validates the modality
- **Creation of Modality**: research that creates and/or refines a tangible modality
- **Preclinical Development**: research that refines the modality for safety, quality, etc.
- **Clinical Trials**: early stage testing in people

The overarching **Supporting Tools** phase represents research on tools, techniques, or processes that support the research conducted in the four phases.

The Credentialing phase is distinct from basic discovery—it requires that the research project confirm a discovery and validate its potential clinical utility. Some specific research projects **included** as translational were:

- establishing mitochondrial markers as valid predictors of treatment outcomes in human cervical cancer patients with known outcomes
- testing the inhibition of specific protein precursors on the prevention and treatment of hepatic micrometastases
- using non-invasive methods to determine if genetic signatures can be reliably identified in glioma cells

Examples of discovery projects **excluded** from the study were:

- identifying the role of a specific protein kinase in signalling pathways that control cell death
- exploring DNA profiles of lung cancer cells to identify a list of genes that may contribute to the aggressiveness of lung cancer (a preliminary fishing expedition)
- determining the early genetic events in retinoblastoma

Details about the kinds of research coded to each modality-phase combination are provided on the following pages.

RISK ASSESSMENT MODALITIES

RA-I. Biospecimen-based

Biospecimen-based RA modalities (also known as biomarkers) are protocols, reagents, or devices/instruments that reveal cancer risk from analysis of blood and/or tissues, the presence of a specific cancer or recurrent cancer, the stage or severity of a specific cancer, and how well the body responds to therapeutic intervention(s). Table 2.2.1 outlines examples of research for each phase within the pathway.

TABLE 2.2.1

RA-I. BIOSPECIMEN-BASED [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Discover molecular biomarker with clinical potential • Validate biomarker (confirm sensitivity/specificity expected for clinical utility) • Assess feasibility of development of protocol/reagent/device
2 – CREATION OF MODALITY	• Define patient subset with biomarker using small number of specimens in a single laboratory • Validate assay and correlation of biomarker with outcomes retrospectively across large number of specimens in different labs
3 – PRECLINICAL DEVELOPMENT	• Develop/refine clinical grade biomarker assay protocol/reagent/device • Validate in prospective human study of biomarker correlation with outcome
4 – CLINICAL TRIALS	• Study in humans of utility of biomarker to direct therapy or chemoprevention or predict outcome/risk
SUPPORTING TOOLS	• Develop biospecimen repositories linked with outcomes data for relevant disease • Develop research-grade reproducible assay and standard reagent(s) for biomarker or profile

[1] For more information, see S. Srivastava et al., "Translational Research Working Group developmental pathway for biospecimen-based assessment modalities," *Clinical Cancer Research* 14(18) 2008:5672–5677.

RA-II. Image-based

Image-based RA modalities include devices like magnetic resonance imaging, computed tomography, and positron emission tomography scanners that identify the presence of a specific cancer, the stage or severity of a specific cancer, how well the body responds to treatment(s), and how to plan the most efficacious treatment on the basis of anatomical, functional, or molecular parameters. This category also includes research on imaging agents, contrast agents, imaging enhancers, and therapeutic agents with secondary imaging attributes. In contrast to the other modalities where laboratory research is often the point of entry, translational research on Image-based RA modalities is often characterized by applied research. In addition, approvals for Image-based modalities tend to be more generic (on the basis of overall patient safety/efficacy) and are usually not related to specific clinical utility. Table 2.2.2 provides an overview of the research that is characteristic of the phases in this pathway.

TABLE 2.2.2

RA-II. IMAGE-BASED [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Discover imaging biomarker with clinical potential • Validate biomarker (confirm sensitivity/specificity expected for clinical utility) • Assess feasibility of developing agent or technique
2 – CREATION OF MODALITY	• Develop new imaging platform • Develop new technique/imaging agent • If technique, optimize acquisition of analytic parameters in preclinical or phase I setting • If imaging agent, perform radiolabeling dosimetry
3 – PRECLINICAL DEVELOPMENT	• Test/refine imaging performance, pharmacokinetics/pharmacodynamics (PK/PD), toxicology, etc., in preclinical setting • Establish Good Manufacturing Practice (GMP) production for agent as necessary • Test/refine imaging performance, PK/PD, toxicology, etc., in phase I/II setting • Establish Good Manufacturing Practice (GMP) for platform as necessary • Optimize platform available for clinical testing
4 – CLINICAL TRIALS	• Conduct phase II+ trials for specific clinical utilities
SUPPORTING TOOLS	• Develop new assays or other supporting tools

[1] For more information, see G.S. Dorfman et al., "Translational Research Working Group developmental pathway for image-based assessment modalities," *Clinical Cancer Research* 14(18) 2008:5678–5684.

INTERVENTIVE MODALITIES

INT-I. Agents (Drugs & Biologics)

Agents, the first of the four INT modalities, include small molecules and biological compounds. Research projects that typify the specific phases in this pathway are outlined in Table 2.2.3.

TABLE 2.2.3

INT-I. AGENTS (DRUGS & BIOLOGICS) [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Discover target with clinical potential • Validate target (convincing empirical basis for attributing clinical potential) • Assess feasibility of developing agent against the target
2 – CREATION OF MODALITY	• Assess impact of perturbing target using experimental system • Identify candidate agents and screen for binding and influence on activity • Select lead candidate
3 – PRECLINICAL DEVELOPMENT	• Conduct preliminary toxicology screening • Conduct process development/pilot manufacturing • Verify activity/PK in pilot product • Implement Good Laboratory Practice (GLP)/GMP • Verify activity/pharmacokinetics (PK)/stability/quality control in GLP/GMP product • Perform definitive toxicology screening • Complete Investigational New Drug (IND) submission
4 – CLINICAL TRIALS	• Conduct phase I clinical trial(s) • Conduct phase II clinical trial(s)
SUPPORTING TOOLS	• Identify/develop research-grade reproducible assay for effect of agent on oncogenic activity • Identify/develop clinically or target-relevant cell culture system(s) and/or target-relevant animal model(s) • Develop and validate assay and standard reagents or imaging methods to measure biomarkers of biological response • Develop and validate assay and standard reagents or imaging methods to measure biomarkers of endpoint in humans • Identify or develop biospecimen/image repositories linked with outcomes data for relevant disease • Identify/develop research-grade reproducible assay and standard reagents or imaging methods to measure target • Validate assay or imaging biomarker(s) that define(s) patient cohort likely to respond to agent

[1] For more information, see R.L. Schilsky et al., "Translational Research Working Group developmental pathway for anticancer agents (drugs or biologics)." *Clinical Cancer Research* 14(18) 2008:5685–5691.

INT-II. Immune Response Modifiers

Immune Response Modifiers are immune-based therapies that either stimulate an individual's immune system so that it will recognize and destroy cancerous cells (also known as "active" immunotherapy, which includes vaccines and cytokine therapy), or provide the immune response to the patient (also known as "passive" immunotherapy like monoclonal antibody drugs or adoptive T-cell therapy). Table 2.2.4 outlines the research that characterizes each phase within this pathway.

TABLE 2.2.4

INT-II. IMMUNE RESPONSE MODIFIERS [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Discover antigen or other immune modifier with clinical potential in specific cancer(s) • Validate immune modifier (convincing empirical basis for attributing clinical potential) • Assess feasibility of identifying/developing the immune response modifier
2 – CREATION OF MODALITY	• Characterize and/or modify antigens • Identify or develop delivery vehicle (vector, cell, etc.) • Identify or develop immune modulator (adjuvant, cytokine, chemokine, etc.) • Develop immune response modifier • Measure response to immune response modifier and refine antigen(s), delivery vehicle, immune modulator, as necessary • Refine immune response modifier and/or immunization strategy • Identify lead immune response modifier candidate
3 – PRECLINICAL DEVELOPMENT	• Conduct process development/pilot manufacturing • Verify activity in pilot product • Implement GLP/GMP • Verify activity in GMP/GMP product • Conduct toxicology screening • Complete IND submission
4 – CLINICAL TRIALS	• Conduct phase I clinical trial(s) • Conduct phase II clinical trial(s)
SUPPORTING TOOLS	• Identify/develop clinically or target-relevant cell culture system(s) and/or animal model(s) • Develop/validate assay and standard reagents or imaging biomarkers to measure response to immune response modifier • Develop/validate assay and standard reagents or imaging biomarkers to measure molecular endpoint in humans • Identify/develop research-grade reproducible assay and standard reagents or imaging biomarkers for immune target • Identify/develop biospecimen/image repositories linked with outcomes data • Identify patient subset with immune target • Characterize statistical correlation of target with outcome • Validate assay or imaging biomarkers for identifying patient cohort

[1] For more information, see M.A. Cheever et al., "Translational Research Working Group developmental pathway for immune response modifiers," *Clinical Cancer Research* 14(18) 2008:5692–5699.

INT-III. Interventive Devices

Interventive Devices may target local-regional sites of cancers or precancerous lesions or be delivered in systemic ways (i.e., for treatment of hematological malignancies or metastases). Examples include radiation therapy, cryoablation, radiofrequency or microwave ablation, interstitial laser thermal therapy, photodynamic therapy, high-intensity focused ultrasound, and minimally invasive surgery tools. These modalities may be delivered noninvasively, percutaneously, endoscopically, laparoscopically, transvascularly, or by open surgery. Research focused on the mechanism for guiding/monitoring the device and its effects is also included under this modality, as is research focused on radiobiological modelling and dosimetry. See Table 2.2.5 for an overview of the research that is characteristic of the phases in this pathway.

TABLE 2.2.5

INT-III. INTERVENTIVE DEVICES [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Identify technology innovation or innovative application of existing technology • Validate technology (convincing empirical basis for attributing clinical potential) • Assess feasibility of developing the technology
2 – CREATION OF MODALITY	• Analyze utility of technology in laboratory • Build/refine prototype device • Test prototype on phantoms and/or animals • Define usage protocol for humans
3 – PRECLINICAL DEVELOPMENT	• Build/refine clinical-grade device • Test clinical-grade device on phantoms and/or animals • Conduct phase 0 tests on humans • Prepare regulatory submission
4 – CLINICAL TRIALS	• Conduct phase I trials (proof of principle)
SUPPORTING TOOLS	• Identify/develop reproducible assay and standard reagents or imaging biomarkers for target • Identify/develop biospecimen/image repositories linked with outcomes data • Identify marker(s) that define patient subset with target • Develop/validate assay and standard reagents or imaging biomarkers to measure biological response or molecular endpoint in humans • Characterize statistical correlation of markers with outcomes, select optimal marker or profile • Validate assay or imaging biomarker for identifying patient cohort

[1] For more information, see G.S. Dorfman, T.S. Lawrence, and L.M. Matrisian, "Translational Research Working Group developmental pathway for interventive devices," *Clinical Cancer Research* 14(18) 2008:5700–5706.

INT-IV. Lifestyle Alterations

Although the TRWG includes survivorship research within the Lifestyle Alterations, for the purposes of this report, this modality has been limited to behavioural change interventions used to prevent and/or treat a person's cancer disease status, thus making it more comparable with the other INT modalities. Lifestyle Alterations include stopping tobacco use, increasing physical activity, reducing alcohol intake, modifying diet, limiting sun exposure, and avoiding hazardous occupational exposures. Interventions that involve an assistive agent (e.g., nutritional

supplements, nicotine replacement) or a device (e.g., acupuncture) are also included in this pathway. Descriptions of research that typifies each phase in the Lifestyle Alterations pathway are provided in Table 2.2.6.

TABLE 2.2.6

INT-IV. LIFESTYLE ALTERATIONS [1]

DEVELOPMENTAL PHASE	RESEARCH
1 – CREDENTIALING	• Validate correlation between behaviour or exposure and disease (empirical basis for attributing causal effect consistent across diverse populations/study designs) • Identify specific lifestyle alteration that would mitigate the risk factor
2 – CREATION OF MODALITY	• Specify lifestyle alteration
3 – PRECLINICAL DEVELOPMENT	• Evaluate effect in relevant animal model
4 – CLINICAL TRIALS	• Conduct pilot study to assess efficacy of lifestyle alteration • Refine specification of lifestyle alteration • Conduct study of efficacy in larger, more diverse population
SUPPORTING TOOLS	• Identify target population via existing databases or new studies • Develop and validate biochemical, behavioural, and/or imaging assays to measure effect of lifestyle alteration

[1] For more information, see E.T. Hawk et al., "Translational Research Working Group developmental pathway for lifestyle alterations," *Clinical Cancer Research* 14(18) 2008:5707–5713.

Additional Coding Conventions

For the purposes of this report, investment in equipment and other related infrastructure that is **directly** used in translational research projects was also identified. This category included support for:

- specific equipment
- laboratory set-up/multi-user equipment and other infrastructure, when the principal investigators were actively involved in translational research
- related workshops/conferences
- letters of intent and other research planning/development activities, such as network set-up
- support for clinical trials infrastructure

Funding for clinical trials infrastructure was weighted at 30% and coded to Agents. The weighting was derived from the finding that early-stage clinical trials represented about 30% of the investment of all clinical trials in the CCRS and that the vast majority were drug trials.

Other conventions, designed to clarify issues related to modality coding, were as follows:

- Research on image-guided treatment (e.g., adaptive radiotherapy) was coded to Interventive Devices.
- Research involving radionuclides was coded to Image-based risk assessment when imaging biomarkers were the focus of the research and to Agents when treatment was the focus.

- Research on devices for biopsy and lymphadenectomy was coded under Biospecimen-based RA.
- Research on drug-delivery vehicles (e.g., lipid-based nanoparticles) was coded as Agents and/or Immune Response Modifiers. Where the translational effort was concentrated on a mechanical device for drug delivery, however, the research was coded to Interventive Devices.
- Research on optimizing stem cell and bone marrow transplants was coded to Agents.
- Research on the prevention of cancer-causing infectious agents was coded to Agents and/or Immune Response Modifiers. (As previously mentioned, projects dealing with the treatment of cancer-causing infectious agents were excluded.)

To assess the robustness of the TRWG framework as applied to the CCRS dataset, a primary and a secondary coder classified 194 projects in terms of modality and phase. For modality, the observed agreement between the coders was 92.3%. The Cohen's kappa coefficient (unweighted) was 0.90 (95% confidence intervals 0.84–0.95), indicating "almost perfect agreement." For phase, observed agreement was 79.8% and the Cohen's kappa coefficient (unweighted) was 0.60 (95% confidence intervals 0.49–0.71), indicating "moderate agreement." The two coders discussed discordant coding in order to arrive at a final determination of modality and phase.

2.3 REPORTING CONVENTIONS

The calendar year defines the time frame within the CCRS to standardize the disparate funding cycles of participating organizations to consistent 12-month periods. In this study the investment for each project was based on a prorated calculation that assumed that project dollars were paid in equal monthly instalments in accordance with project start and end dates. Project funding was calculated for the period January 1, 2005 to December 31, 2007, and the three-year totals were averaged to generate annual investments. Figures shown in the tables and charts are rounded and may not always equal the totals shown.

Project budgets are weighted/allocated in a variety of ways, as summarized in Table 2.3.1. Overall, project budgets were weighted from 10% to 100%. Most project budgets (83.8%) were included in full (see Table 2.3.2).

TABLE 2.3.1

EXAMPLES OF WAYS IN WHICH PROJECT BUDGETS WERE WEIGHTED

Issue	Example	Approach
Project is not entirely focused on cancer	"Microwave-acoustic breast tumor detection and design and analysis of wireless implants for neurophysiological research"	Budget was weighted at 50% because the cancer component was assumed to compose half the research activities.
Project does not entirely qualify as early translational research	"Establish the most effective combination chemotherapy with anti-angiogenic factors on osteosarcoma and elucidate the hereditary mechanism of embryonal rhabdomyosarcoma"	Budget was weighted at 50% because the project had an early translational component focusing on novel anti-angiogenic agents, as well as a discovery component focusing on the genetic etiology of rhabdomyosarcoma.
Project involves more than one modality of the TRWG framework	"Combined oncolytic virotherapy and targeted radiotherapy of peritoneal carcinomatosis"	Budget was split between Agents and Interventive Devices.
Project spans more than one phase of the TRWG framework	"Regional delivery of antineoplastic and chemosensitizing agents by polymeric microspheres"	Budget was assigned to both Creation of Modality and Preclinical Development.
Project involves more than one cancer site	"Molecular structures for the optimization of single domain antibodies developed against brain and breast cancer biomarkers"	Budget was allocated to two cancer sites (i.e., brain, breast). Note that predetermined site allocations based on expert input are used for projects dealing with specific risk factors (e.g., tobacco) when cancer sites were not identified.

TABLE 2.3.2

DISTRIBUTION OF WEIGHTINGS APPLIED TO PROJECTS CLASSIFIED AS TRANSLATIONAL CANCER RESEARCH

WEIGHTING	Number of projects	% projects	% investment
10	4	0.2	0.3
20	37	1.8	0.7
25	9	0.4	1.4
30	8	0.4	2.6
33	91	4.4	4.4
50	181	8.9	10.7
66	1	0.1	1.3
75	4	0.2	0.3
100	1,708	83.6	78.3
TOTAL	**2,043**	**100**	**100**

The institutional affiliation of the nominated principal investigator was used for analyses based on geography (both province and city). There is only one nominated principal investigator per project. Components of multi-component projects are considered individual projects if the funding organization provided details (i.e., description, researchers, budget, etc.) on the component parts. The Canadian Breast Cancer Research Alliance (CBCRA), the Canadian Cancer Society, National Research Council Canada, Ontario Institute for Cancer Research, and The Terry Fox Foundation provided this level of detail. For clinical trials supported by the Canadian Cancer Society, each site involved in the trial is treated as a separate project with its own principal investigator and budget (based on per case and site administration funding).

All projects are coded to cancer sites using the ICD-10 in accordance with the level of detail provided in the project description. ICD-10 codes are rolled up to 24 cancer sites. Collectively, these cancer sites represent ~90% of all new cancer cases and deaths per year. Individually, each represents a weighted average of at least 0.3% of all new cancer cases and deaths in a given year.

In contrast to the separate reporting of the three multi-funded initiatives used in previous CCRA reports, investments in the Canadian Prostate Cancer Research Initiative and the Canadian Tobacco Control Research Initiative (CTCRI) were included in the figures of the relevant funder organizations. This is also the case for CBCRA for investments made by the Canadian Breast Cancer Foundation, the Canadian Cancer Society, the Canadian Institutes of Health Research, the Health Canada/Public Health Agency of Canada, and The Cancer Research Society. Investments made by Avon Canada, the Breast Cancer Society of Canada, and the CURE Foundation, however, are summed and included under CBCRA, which is listed under the voluntary sector.

2.4 LIMITATIONS

This study shares the same limitations as the CCRS. The CCRS captured data on projects funded on the basis of peer review and often in response to publicly announced research granting competitions. It was not designed to include all intramural translational cancer research supported by federal and provincial governments/agencies or by universities, hospitals, or cancer centres. Although there has been an attempt to include research funding by hospital foundations, to date, no data has been obtained. In addition, the BC Cancer Agency did not contribute data to the CCRS during the reporting period so the figures shown for British Columbia may under-represent the level of early translational cancer investment for the province.

Research undertaken by industry is also not part of the CCRS database. As noted in chapter 1, industry investment in the preclinical and early trials phases of translational research is substantial.

Beyond issues related to the scope of the survey, it is also worth mentioning that project classification is highly dependent on the quality of the research descriptions provided by the funding organizations. Disagreements between the primary and secondary coders often occurred because the source descriptions were limited or poor. Coding to phase was most susceptible to poor project descriptions.

And finally, it is recognized that there may be issues related to the study's methodology. The inclusion of validated discovery within the definition of the Credentialing phase in the TRWG framework is somewhat controversial. In NCI's own pilot work involving the framework, there was concern that the translational relevance of its research investment may have been overstated. There are also concerns that the inclusion of Lifestyle Alterations was a forced fit and did not readily belong in what was traditionally construed as biomedical/clinical translational research. The separation of Immune Response Modifiers from other Agents, while justified by the TRWG because of their primary mode of action and the inherent methodological challenges of immune response research, is a fairly arbitrary distinction. Furthermore, the exclusion of investment in training/capacity building and stand-alone biospecimen banks/repositories and platforms, which are important foundations for translational research, may have understated the extent of the investment. To address these issues, the findings have been stratified so that readers can access those investment figures meaningful to their own work and information needs.

3. Results

3.1 OVERALL INVESTMENT

Investment in early translational research as defined by the TRWG framework totalled $305.1M over the 2005–2007 period, which represented 26.7% of the overall investment of $1,143.2M in cancer research, a proportion consistent for each of the three years. The average annual investment in translational research was $101.7M.

In terms of the TRWG development pathways paradigm, 34.0% of the investment ($34.6M per year) was for RA, research intended to characterize the cancer-related health status of an individual, including prognostic or predictive biomarkers. The remaining 66.0% of the investment ($67.1M per year) was for INT, research intended to change the cancer-related health status of an individual via prevention or treatment.

One dollar of every five dollars of the translational research investment was for projects dealing with Biospecimen-based RA ($22.2M per year). Most of the Biospecimen-based RA research investment was in the Credentialing phase (32.1% or $7.1M annually), and, in fact, this investment represented 63.3% of the overall investment in Credentialing. Another 23.5% ($5.2M) of the Biospecimen-based RA research investment was for projects focused on developing supporting tools, such as repositories, assays, and reagents within the context of specific translational research projects (as noted, stand-alone biospecimen banking projects were excluded from the investment calculation). The Biospecimen-based RA research investment in Supporting Tools, in fact, represented 62.0% of the total translational research investment in this phase.

Image-based RA represented 12.1% of the overall translational research investment ($12.3M per year). Nearly half of this investment (47.9% or $5.9M annually) was for projects funding equipment and other infrastructure. Another 42.8% ($5.3M) was for projects in the Creation of Modality phase. Investment in the other phases represented less than 10% of total Image-based RA research investment.

In terms of INT, research on Agents totalled $46.5M annually and represented nearly half (45.8%) of the overall translational research investment. Most of the investment in Agents was for projects in the Creation of Modality phase (54.4% or $25.3M per year) with another substantial proportion for projects that funded Other Equipment/infrastructure (22.2% or $10.3M annually). Given the large translational research investment in Agents, this modality had the highest proportion of phase-specific investment for Creation of Modality, Preclinical Development, and Clinical Trials, and Other Equipment/infrastructure.

Investment in research on Immune Response Modifiers at $8.9M annually, represented 8.7% of the overall translational research investment. Much of this investment was for projects in the Creation of Modality phase (44.5% or $4.0M per year). Other Equipment/infrastructure represented another 17.8% ($1.6M annually) of this modality-specific investment.

Research on Interventive Devices totalled $9.8M annually, representing 9.6% of the overall translational research investment. Nearly half of this investment was for Other Equipment/infrastructure (47.6% or $4.7M per year). Another 38.0% of the investment ($3.7M per year) was in the Creation of Modality phase.

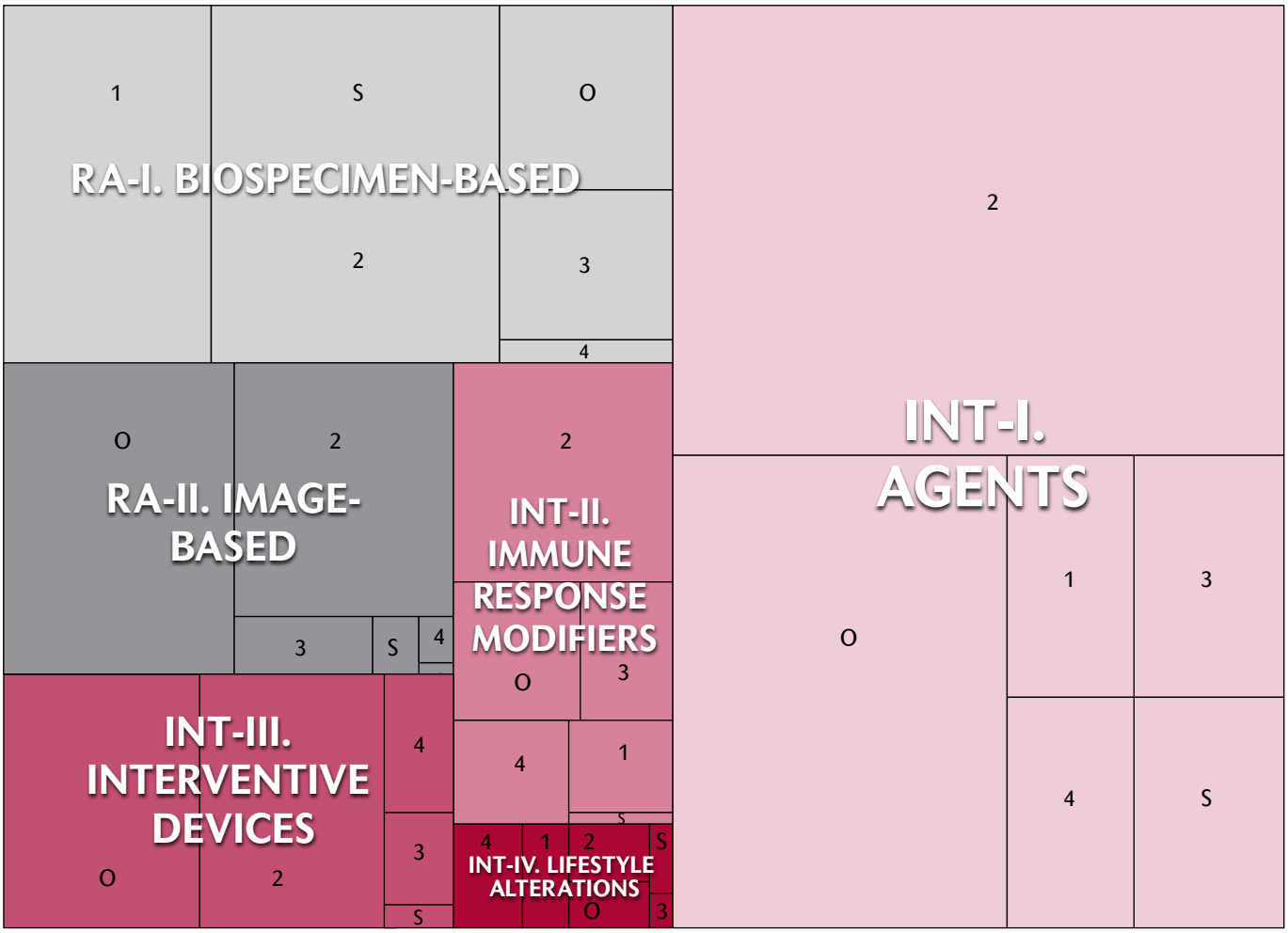
Lifestyle Alterations, at $1.9M per year, formed the smallest proportion of the investment—1.9% overall. The largest proportion of this modality-specific investment was for the Clinical Trials phase (30.6% or $0.6M per year), which for this modality, included pilot and other kinds of efficacy studies. Investment in Credentialing (21.4% or $0.4M per year) and Other Equipment/infrastructure (15.9% or $0.3M per year) represented the second and third highest proportions, respectively.

These data are summarized in the treemap[10] and accompanying data table (see Figure 3.1.1). This graph readily illustrates the concentration of the investment in research on Agents and how the investment in the phase, Creation of Modality, and Other Equipment/infrastructure comprised large components of the investment for most modalities. The small investment in Lifestyle Alterations is also very obvious from the treemap. Detailed investment figures for each modality-phase combination are provided in Appendix B.

10. Treemapping is a method of area-based visualization that uses nested quadrangles to summarize large amounts of hierarchically organized data. Each translational modality (tree branch) is illustrated by a quadrangle, which is then tiled with smaller quadrangles (sub-branches) representing the translational phases.

FIGURE 3.1.1

DISTRIBUTION OF THE AVERAGE ANNUAL INVESTMENT BY MODALITY AND PHASE



1 - CREDENTIALING **2** - CREATION OF MODALITY **3** - PRECLINICAL DEVELOPMENT **4** - CLINICAL TRIALS **S** - SUPPORTING TOOLS **O** - OTHER EQUIPMENT/ INFRASTRUCTURE

Generated using Treemap 4.1 software using the squarified tiling algorithm (see http://www.cs.umd.edu/hcil/treemap).

	MODALITY						
	RISK ASSESSMENT (RA)		INTERVENTIVE (INT)				
DEVELOPMENTAL PHASE	I. Biospecimen-based	II. Image-based	I. Agents	II. Immune Response Modifiers	III. Interventive Devices	IV. Lifestyle Alterations	TOTAL [1]
1 - CREDENTIALING	$7.1M	Less than $0.1M	$2.8M	$0.9M	Less than $0.1M	$0.4M	$11.3M
2 - CREATION OF MODALITY	$4.4M	$5.3M	$25.3M	$4.0M	$3.7M	$0.4M	$43.0M
3 - PRECLINICAL DEVELOPMENT	$2.3M	$0.7M	$3.4M	$1.2M	$0.5M	Less than $0.1M	$8.3M
4 - CLINICAL TRIALS	$0.3M	$0.2M	$2.1M	$1.1M	$0.7M	$0.6M	$5.0M
SUPPORTING TOOLS	$5.2M	$0.2M	$2.6M	Less than $0.1M	$0.2M	$0.2M	$8.5M
OTHER EQUIPMENT/ INFRASTRUCTURE [2]	$2.8M	$5.9M	$10.3M	$1.6M	$4.7M	$0.3M	$25.6M
TOTAL	**$22.3M**	**$12.3M**	**$46.5M**	**$8.9M**	**$9.8M**	**$1.9M**	**$101.7M**

[1] Averaged over the three-year period, 2005–2007.

[2] This included $22.1M (86.5%) for multi-user equipment/lab set-up and other infrastructure, $2.4M (9.3%) for clinical trials infrastructure, $0.5M (2.2%) for specific equipment, $0.5M (1.8%) for research planning/network support/letters of intent, and less than $0.1M (0.2%) for workshops/conferences.

Figure 3.1.2 shows the translational research phases in terms of the overall cancer research investment. The smallest pieces of the pie are the Preclinical Development and Clinical Trials phases, which combined represented $13.3M per year.

FIGURE 3.1.2

DISTRIBUTION OF AVERAGE ANNUAL CANCER RESEARCH INVESTMENT BY TRANSLATIONAL PHASE, 2005-2007

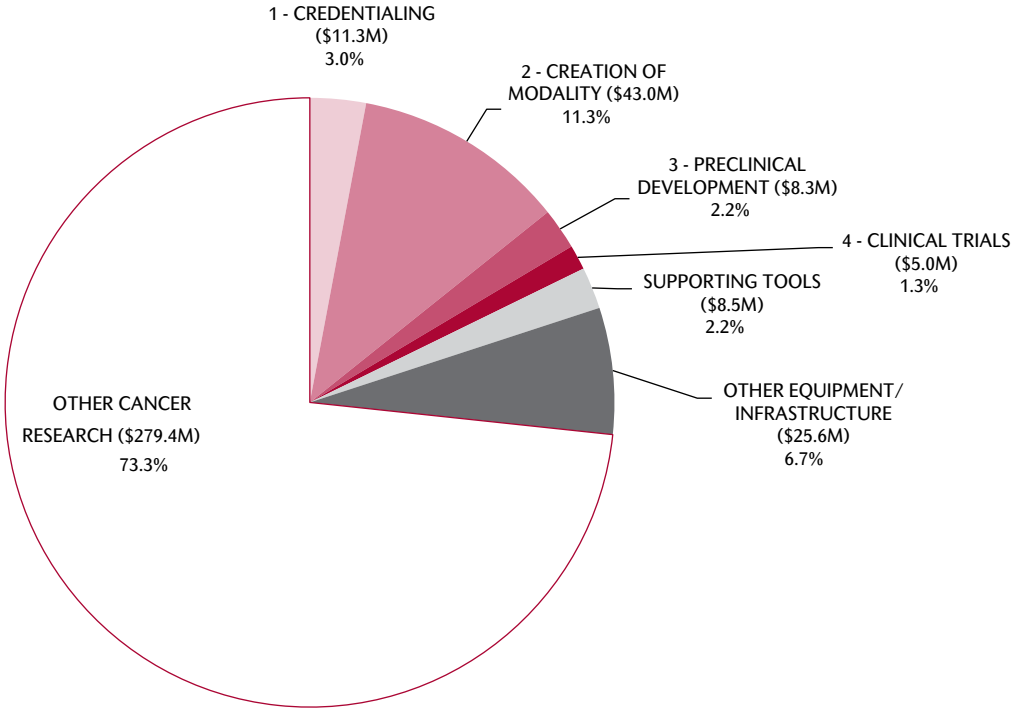


Figure 3.1.3 presents the translational research investment in terms of funding mechanisms, contrasting it with the overall cancer research investment. Operating grants accounted for 63.9% of the overall translational research investment ($65.0M per year), a much larger proportion than found for the overall cancer research investment. Grants for equipment/infrastructure represented 24.0% of the translational research investment ($24.4M per year), but nearly one-third of the overall cancer research investment. Trainee awards and career awards were proportionately smaller in terms of the translational research investment than the overall cancer research investment.

In terms of modalities, operating grants comprised over half of the modality-specific investments for Biospecimen-based RA, Agents, Immune Response Modifiers, and Lifestyle Alterations. For Image-based RA and Interventive Devices, equipment/infrastructure grants formed the largest proportion of the investment. The proportion of modality-specific investment in trainee awards ranged from a low of 2.7% (Biospecimen-based) to a high of 8.3% (Lifestyle Alterations); the proportion of career awards ranged from a high of 10.2% (Agents) to a low of 3.6% (Biospecimen-based).

FIGURE 3.1.3

AVERAGE ANNUAL INVESTMENT IN TRANSLATIONAL CANCER RESEARCH BY FUNDING MECHANISM, 2005–2007

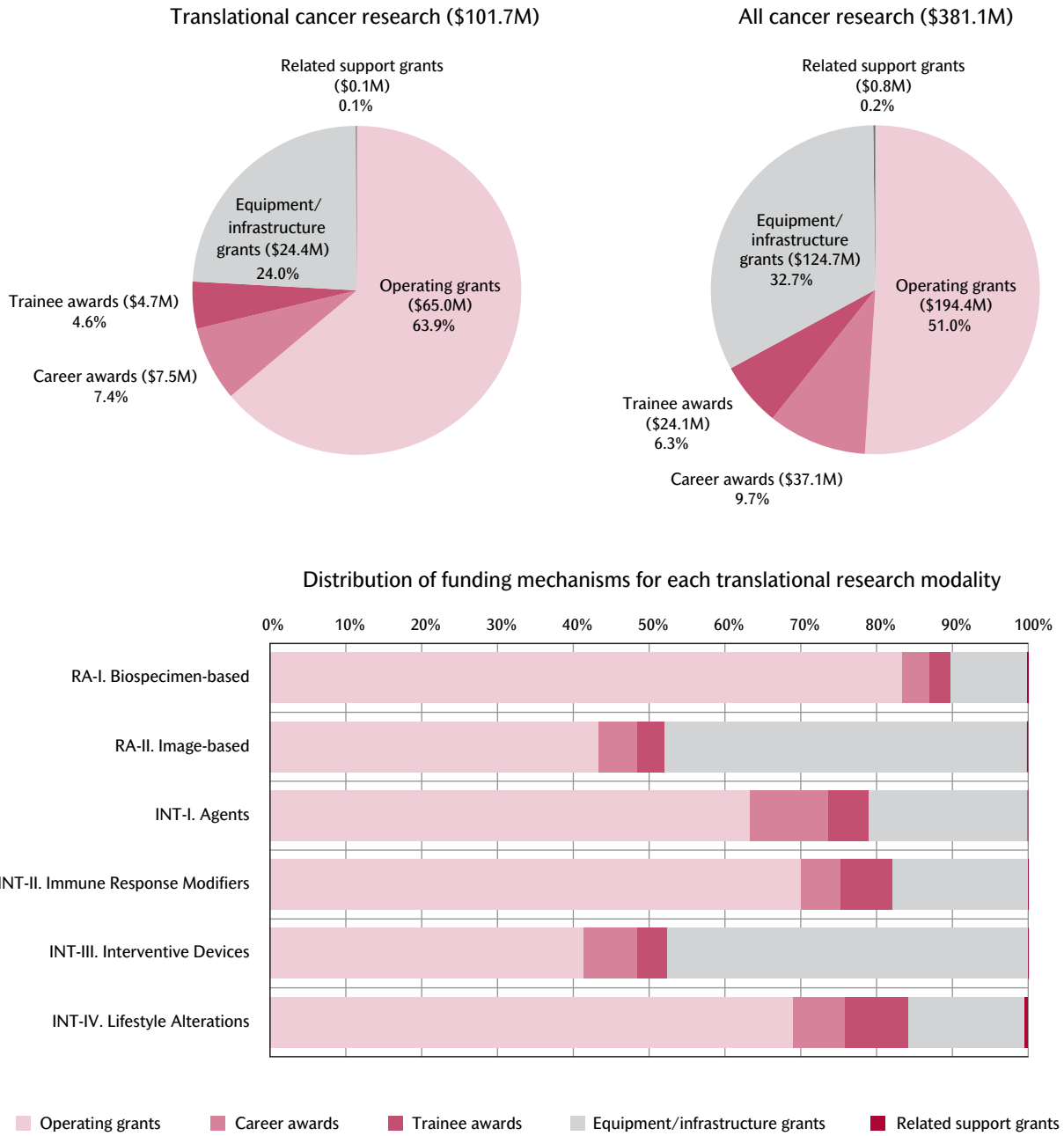
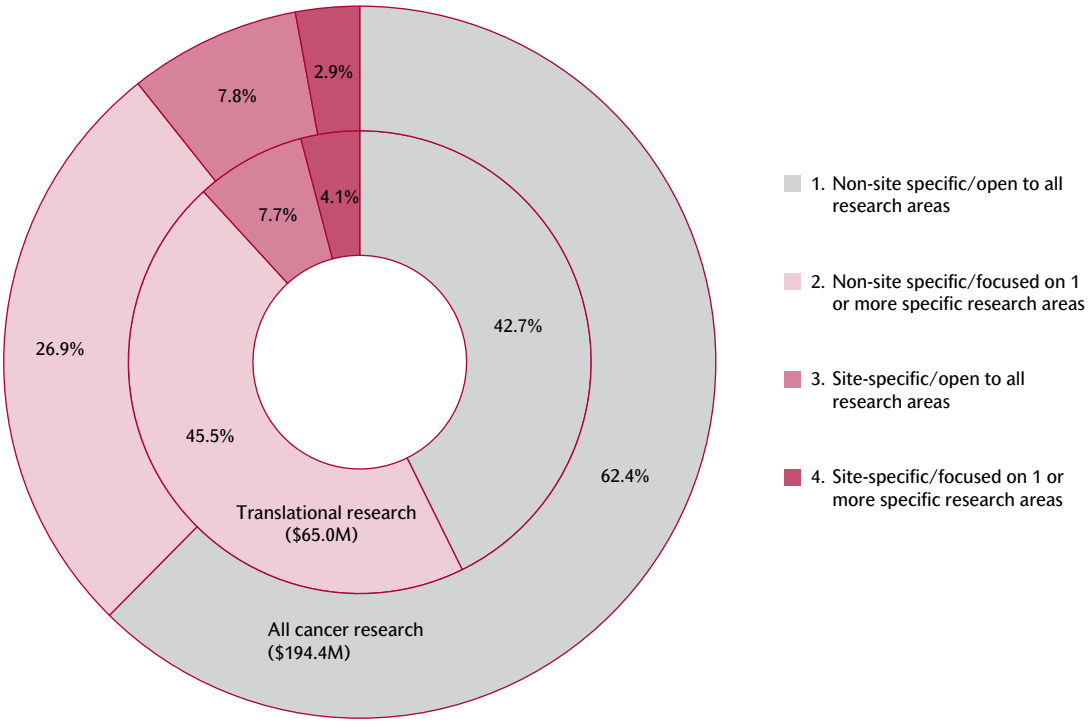


Figure 3.1.4 shows the distribution of operating grants by strategic focus using the four categories from the CCRA annual publication on cancer research investment. A comparatively higher proportion of the translational research investment was focused/strategic (groups 2 and 4). Notably, investments from projects administered by Genome Canada and the Ontario Institute for Cancer Research at $7.7M and $7.5M per year, respectively, accounted for 47.1% of the total investment in strategic operating grants in translational research.

FIGURE 3.1.4

DISTRIBUTION OF AVERAGE ANNUAL RESEARCH INVESTMENT IN OPERATING GRANTS BY FOCUS



Although not included within the investment figures, research funding that supports training/capacity building and research platforms, such as biospecimen banks, makes possible the conduct of translational research. These projects and their funders are listed in Table 3.1.1 and represent an investment of approximately $4M to $5M per year.[11]

11. This listing contains only projects funded by the organizations participating in the CCRS determined to be cancer relevant. Repositories focused on other diseases that may be relevant to and used in cancer research were not reported to the CCRS.

TABLE 3.1.1

CAPACITY BUILDING AND BIOSPECIMEN BANKING PROJECTS EXCLUDED FROM THE TRANSLATIONAL RESEARCH INVESTMENT CALCULATION

TYPE OF PROJECT	ORGANIZATION	PROJECT TITLE
CAPACITY BUILDING/ TRAINING	Canadian Institutes of Health Research	• An integrated cancer research training initiative at Dalhousie University in Nova Scotia (in partnership with Cancer Care Nova Scotia) • CIHR Strategic Training Program in Chemical Biology at McGill University (in partnership with the Fonds de la recherche en santé du Québec) • CIHR/STIHR Partners in Experiential Learning at The University of Western Ontario • Clinician scientists in molecular oncologic pathology program at the University of Toronto • London Strategic Training Initiative in Cancer Research and Technology Transfer (in partnership with Cancer Care Ontario) • Montreal Centre for Experimental Therapeutics in Cancer (in partnership with the Fonds de la recherche en santé du Québec) • Queen's University Transdisciplinary Training Program in Cancer Research (in partnership with The Cancer Research Society) • Research excellence in radiation medicine for the 21st century at Princess Margaret Hospital/ University Health Network (in partnership with Cancer Care Ontario) • The Alberta Cancer Board Training Program in Translational Cancer Research in a partnership with the University of Alberta and the University of Calgary • The Institut de recherches cliniques de Montréal (IRCM) training program in cancer research: From genomics to molecular therapy (in partnership with The Cancer Research Society) • Tobacco use in special populations research training program at The Centre for Addiction and Mental Health
	Canadian Cancer Society (through the Canadian Prostate Cancer Research Initiative)	• The Prostate Centre at Vancouver General Hospital • The Prostate Cancer Group, Princess Margaret Hospital/University Health Network
TUMOUR/TISSUE BANKS & RESEARCH PLATFORMS	Alberta Cancer Research Institute	• PolyomX Initiative
	Brain Tumour Foundation of Canada	• Brain Tumour Tissue Bank at London Health Sciences Centre
	Canada Foundation for Innovation	• Canadian Centre for Applied Cancer Genetics at The Hospital for Sick Children (in partnership with the Ontario Ministry of Research & Innovation) • Network of tissue banks and data for breast and ovarian cancers at the Université de Montréal (in partnership with the Fonds de la recherche en santé du Québec)
	Canadian Breast Cancer Foundation	• Canadian Breast Cancer Foundation Alberta Research Tumor Bank
	Canadian Institutes of Health Research	• Canadian Tumour Repository Network (CTRNet) • The Manitoba Tumor and Breast Tumor Banks at the University of Manitoba
	Fonds de la recherche en santé du Québec	• Réseau de recherche en cancer/Cancer Research Network, which includes the Leukemia Cell Bank, the Tissue and Data Bank, and the Experimental Therapies program
	Michael Smith Foundation for Health Research	• BC BioLibrary at the University of British Columbia • BC Clinical Genomics at the University of British Columbia • Tumour Tissue Repository at the BC Cancer Agency
	Ontario Institute for Cancer Research	• Ontario Tumour Bank
	Ovarian Cancer Canada	• National Ovarian Cancer Tissue Bank at Centre de recherche du CHUM - Pav. Notre-Dame, University of British Columbia, and University of Ottawa

3.2 ORGANIZATION-SPECIFIC INVESTMENT

Almost every organization had some proportion of its cancer research investment classified to the translational research paradigm. Federal government organizations/programs accounted for 60.1% of the investment, and voluntary organizations, provincial health research organizations, and provincial cancer agencies accounted for 21.7%, 13.5%, and 4.7%, respectively. Organizations with investments representing more than 5% of the total annual translational research investment were: Canadian Institutes of Health Research ($24.3M), Canada Foundation for Innovation ($17.1M), Canadian Cancer Society ($10.0M), Ontario Institute for Cancer Research ($9.4M), Genome Canada ($7.7M), and The Terry Fox Foundation ($6.5M) (see Figure 3.2.1A). The proportion of cancer research that was translational ranged from a low of 0% (Fondation du cancer du sein du Québec/Quebec Breast Cancer Foundation) to a high of 100% (National Research Council Canada, which includes all 15 component projects of the Genomics and Health Initiative Program[12]). For nine organizations, investment in early translational research accounted for more than 50% of their overall investment in cancer research (see Figure 3.2.1B).

The distribution of each organization-specific investment in terms of the translational research modalities is summarized in Figure 3.2.2. Although the investment in Agents represents a sizable proportion for many organizations, this is not the case for all organizations.

The density map shown in Figure 3.2.3 shows the details of the organization-specific investment across the six translational modalities. In terms of Biospecimen-based RA research, Genome Canada accounted for 34.5% of the investment ($7.7M annually). Canada Foundation for Innovation represented the largest proportions of the investments for Image-based RA research (36.9% or $4.5M) and Interventive Devices (42.4% or $4.1M). The Canadian Institutes of Health Research had the largest proportions of the investments for Agents (31.3% or $14.5M), Immune Response Modifiers (at $2.4M or 26.9%), and Lifestyle Alterations (at $0.6M or 34.2%).

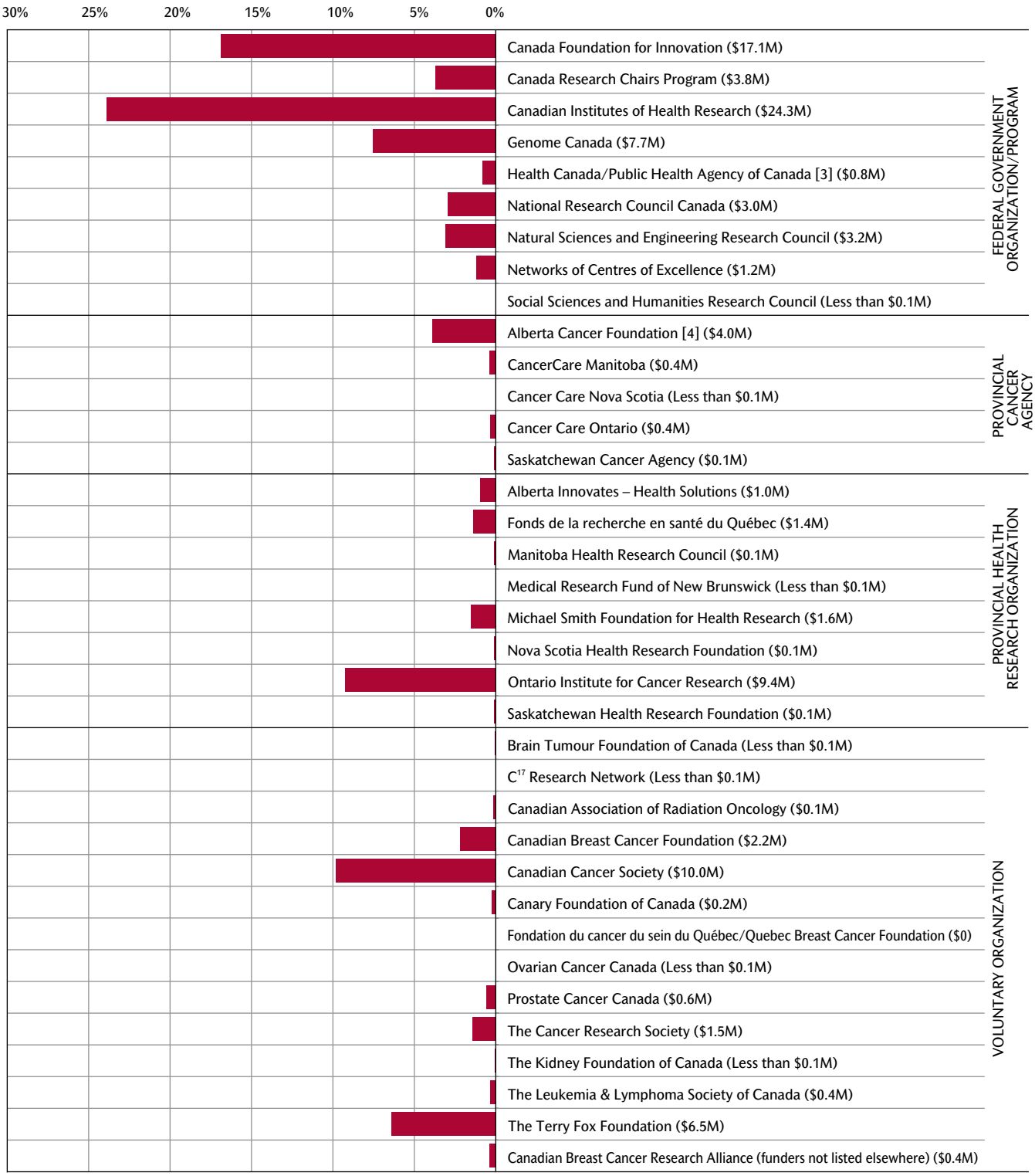
Phase-specific investments for each organization are provided in Appendix C. Nearly 70% of the investment in the Preclinical Development phase was represented by Canadian Institutes of Health Research ($3.3M per year), Genome Canada ($1.3M per year), and Ontario Institute for Cancer Research ($1.3M per year). Two-thirds of the investment in Clinical Trials was represented by the Ontario Institute for Cancer Research ($1.2M per year), Canadian Institutes of Health Research ($1.1M per year), and the Canadian Cancer Society ($1.0M per year).

12. Other cancer research conducted at the National Research Council Canada is not peer-reviewed in the same way as the Genomics and Health Initiative Program and is not reported to the CCRS.

FIGURE 3.2.1

AVERAGE ANNUAL INVESTMENT IN TRANSLATIONAL CANCER RESEARCH BY FUNDING ORGANIZATION, 2005–2007

A. Distribution of investment in translational cancer research across funding organizations [1]



[1] Initiative investment is allocated to the appropriate organization. Denominator is $101.7M.
[2] Individual funder denominators are shown in brackets.
[3] Represents investment in the initiatives.
[4] In 2010, Alberta Cancer Foundation became the direct funding agency for funding programs administered by the former Alberta Cancer Board.

B. Proportion of cancer research investment that is translational for each funding organization [2]

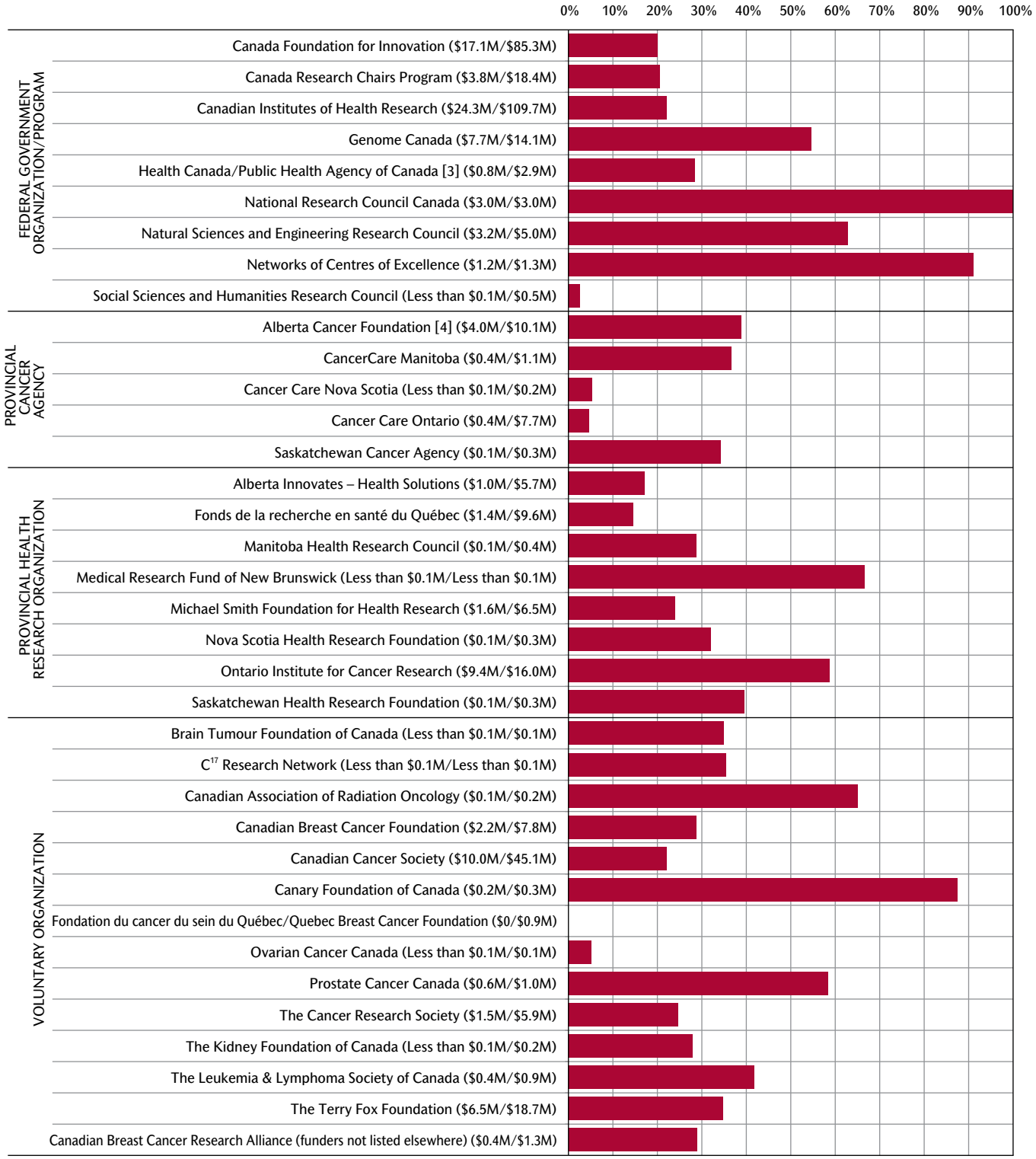
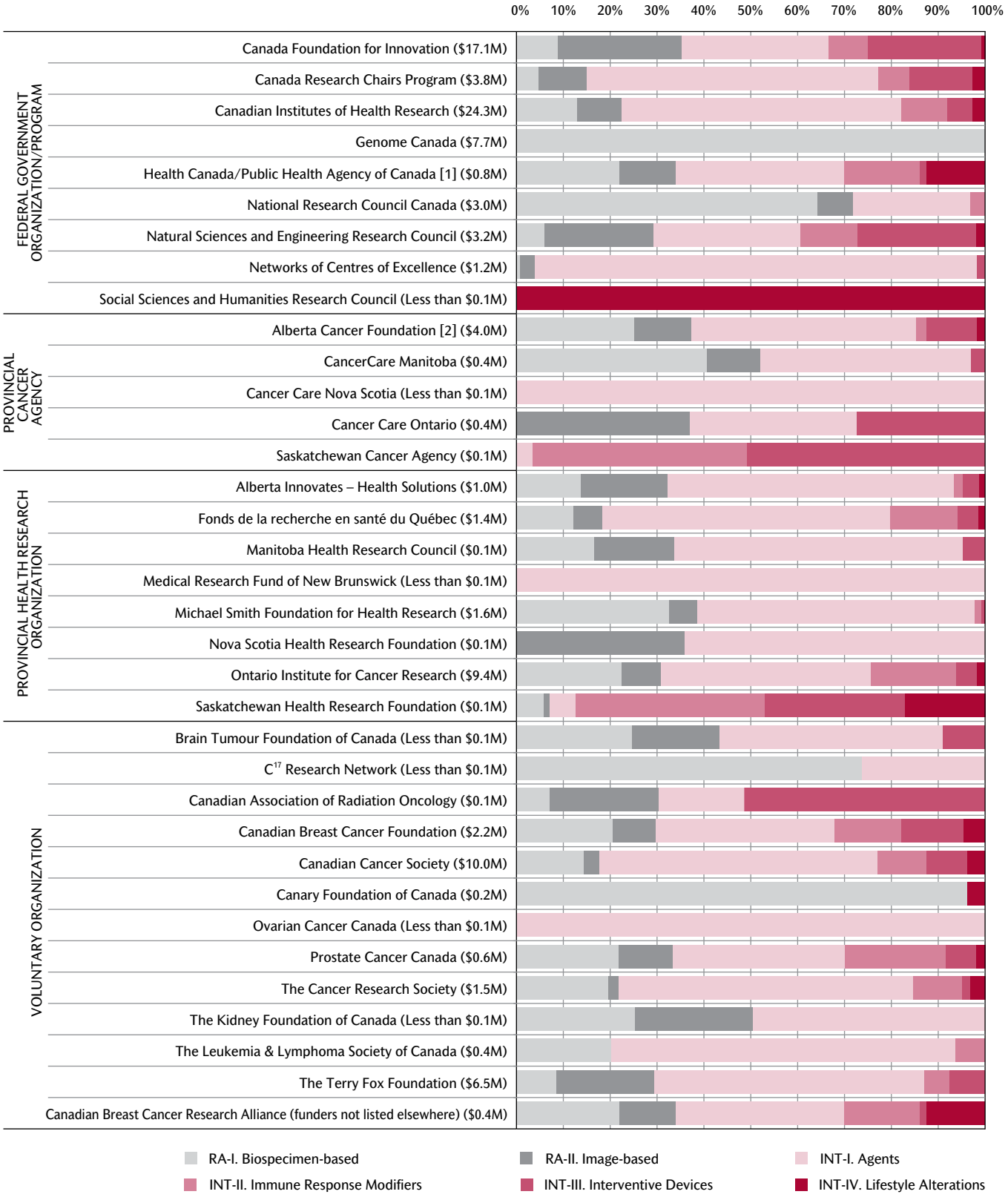


FIGURE 3.2.2

DISTRIBUTION OF AVERAGE ANNUAL INVESTMENT IN TRANSLATIONAL CANCER RESEARCH BY MODALITY FOR EACH FUNDING ORGANIZATION, 2005–2007 ($101.7M)



[1] Represents investment in the initiatives.
[2] In 2010, Alberta Cancer Foundation became the direct funding agency for funding programs administered by the former Alberta Cancer Board.

FIGURE 3.2.3

AVERAGE ANNUAL TRANSLATIONAL CANCER RESEARCH INVESTMENT BY MODALITY AND FUNDING ORGANIZATION, 2005–2007 ($101.7M)

[1] Represents investment in the initiatives.
[2] In 2010 Alberta Cancer Foundation became the direct funding agency for funding programs administered by the former Alberta Cancer Board.

3.3 INVESTMENT BY PROVINCE AND CITY

The investment in translational research was examined in terms of the province (see Table 3.3.1). The most populous provinces had the largest overall cancer research investments and the highest levels of investment in translational research. As principal investigators based in Ontario received nearly half of the overall cancer research investment, so too did they receive the largest amount of the translational research investment (46.8% or $47.2M annually).

Of the overall cancer research investment in Newfoundland & Labrador, 10.4% was translational (i.e., 6/35 projects during the 2005–2007 period). In contrast, the investment in translational research exceeded 35% of the overall cancer research investment in Prince Edward Island, Saskatchewan, and British Columbia. It is noteworthy that British Columbia represented a much higher proportion, and Quebec a much lower proportion, of the translational research investment when compared with the provincial distribution of the overall cancer research investment.

TABLE 3.3.1

AVERAGE ANNUAL TRANSLATIONAL CANCER RESEARCH INVESTMENT BY PROVINCE, 2005–2007 ($100.9M) [1, 2]

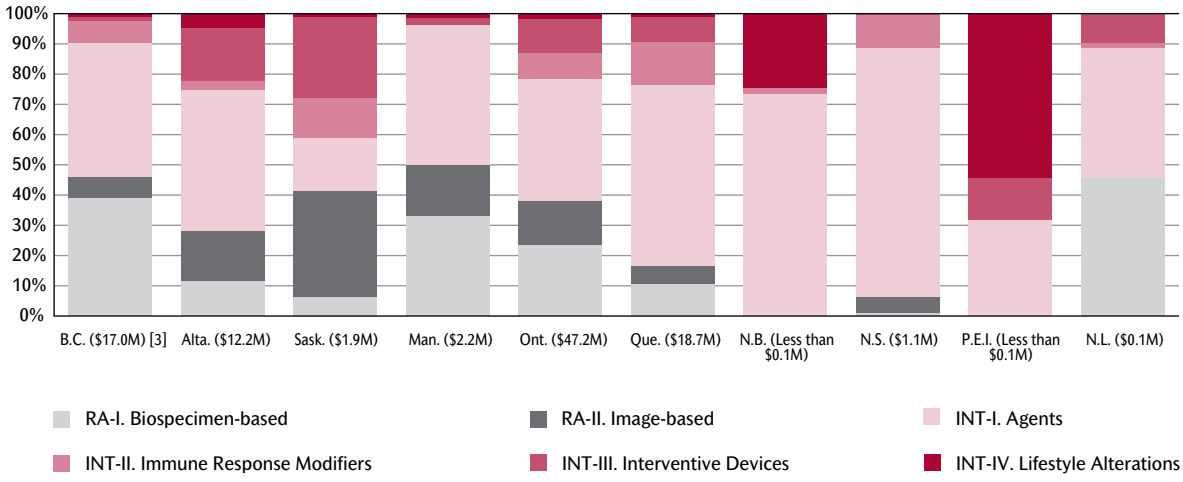
	B.C. [3]	Alta.	Sask.	Man.	Ont.	Que.	N.B.	N.S.	P.E.I.	N.L.
Average annual translational research investment	$17.5M	$12.2M	$1.9M	$2.2M	$47.2M	$18.7M	Less than $0.1M	$1.1M	Less than $0.1M	$0.1M
Average annual cancer research investment	$44.5M	$36.5M	$4.7M	$8.5M	$181.1M	$96.0M	$0.2M	$5.1M	$0.1M	$1.0M
% of cancer research investment that is translational	39.2%	33.3%	40.4%	25.9%	26.1%	19.5%	33.4%	21.2%	49.3%	10.4%
Provincial distribution of the translational research investment	17.3%	12.0%	1.9%	2.2%	46.8%	18.5%	0.1%	1.1%	0.1%	0.1%
Provincial distribution of the cancer research investment	11.8%	9.7%	1.2%	2.2%	47.9%	25.4%	0.1%	1.3%	Less than 0.1%	0.3%

[1] Excludes awards to trainees who were at institutions outside Canada.
[2] The location of the nominated principal investigator's institution is used to assign investment to specific provinces.
[3] BC Cancer Agency data are not included and figures may underestimate the investment in B.C.

The distribution of translational research investment in terms of modality varied from province to province (see Figure 3.3.1). Biospecimen-based RA represented more than 20% of the investments in British Columbia, Manitoba, Ontario, and Newfoundland & Labrador. For Saskatchewan, 34.9% of the investment was in Image-based RA, more than double the proportion of any other province. The proportion of investment in Interventive Devices at 26.6% in Saskatchewan also exceeded all other provinces. While for most provinces, a sizable proportion of the investment was for Agents, the highest proportion was for Nova Scotia at 82.2%.

FIGURE 3.3.1

DISTRIBUTION OF AVERAGE ANNUAL INVESTMENT IN TRANSLATIONAL RESEARCH BY MODALITY, PROVINCES [1,2] ($100.9M)



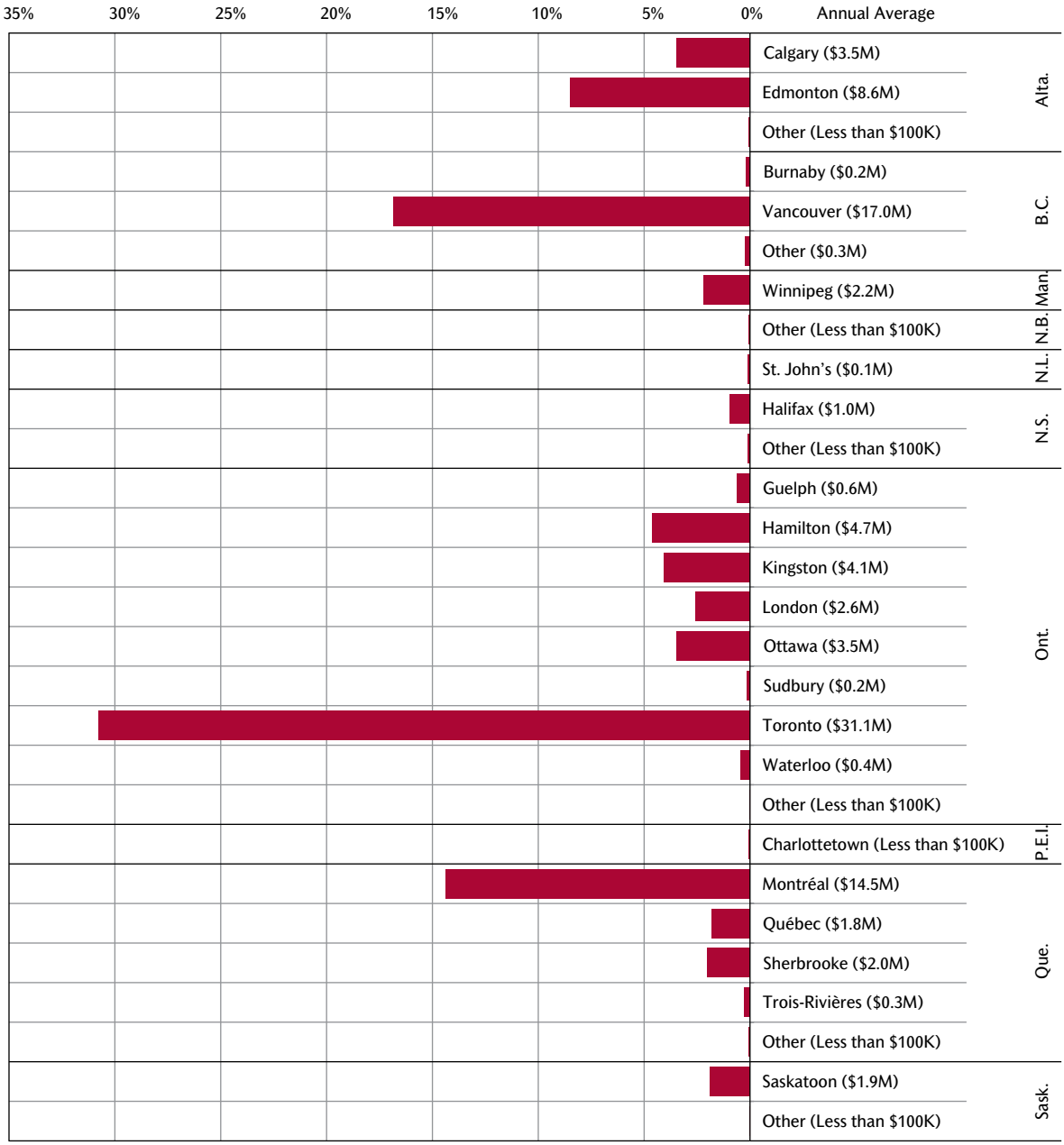
[1] Excludes awards to trainees who were at institutions outside Canada.
[2] The location of the nominated principal investigator's institution is used to assign investment to specific provinces.
[3] BC Cancer Agency data are not included.

Translational research funding went to principal investigators working at institutions located in 39 Canadian cities. Over 70% (70.5%) of the annual investment went to researchers in four cities—Toronto ($31.1M), Vancouver ($17.0M), Montreal ($14.5M), and Edmonton ($8.6M). (These same cities combined represent the same proportion of the overall cancer research investment.) The overall distribution of translational funding by cities is presented in Figure 3.3.2A alongside the modality distributions for each city (Figure 3.3.2B).

FIGURE 3.3.2

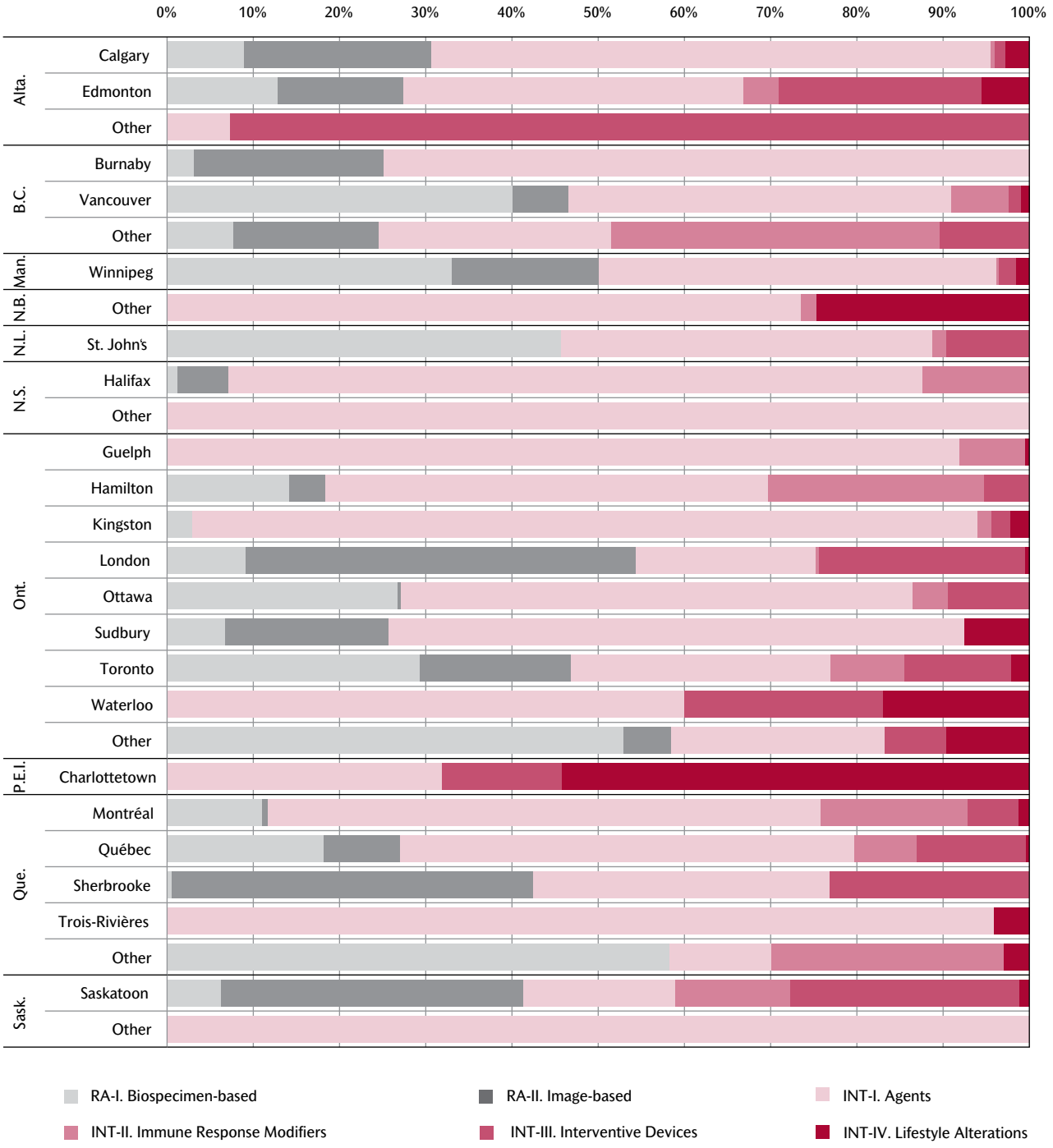
AVERAGE ANNUAL INVESTMENT IN TRANSLATIONAL CANCER RESEARCH BY CITY [1,2], 2005–2007

A. Distribution of investment in translational cancer research across cities



[1] The location of the nominated principal investigator's institution is used to assign investment to specific cities.
[2] Only cities with an average annual investment greater than $100,000 are listed.

B. Distribution of translational cancer research investment by modality for each city



The phase-specific investments for each city are provided in Appendix D. A snapshot of the investment in Preclinical Development and Clinical Trials by key cities is shown in Table 3.3.2.

TABLE 3.3.2

DISTRIBUTION OF THE INVESTMENT IN PRECLINICAL DEVELOPMENT AND CLINICAL TRIALS BY CITY, 2005–2007

PROVINCE	CITY	3 - PRECLINICAL DEVELOPMENT		4 - CLINICAL TRIALS	
		Investment [1] (millions of dollars)	%	Investment [1] (millions of dollars)	%
B.C. [2]	Vancouver	1.5	18.3	0.4	8.2
Alta.	Calgary	0.1	1.2	0.2	5.1
	Edmonton	0.8	9.7	0.3	6.6
Ont.	Hamilton	0.2	2.6	0.7	15.1
	Toronto	3.3	40.1	2.4	50.2
Que.	Montréal	1.2	14.5	0.5	9.6
	Sherbrooke	0.4	4.8	0	0
Other	Other cities	0.1	8.7	0.1	5.3
TOTAL		**7.6**	**100**	**4.6**	**100**

[1] Averaged over the three-year period, 2005–2007.

[2] BC Cancer Agency data are not included and figures may underestimate the investment in B.C.

3.4 SITE-SPECIFIC INVESTMENT

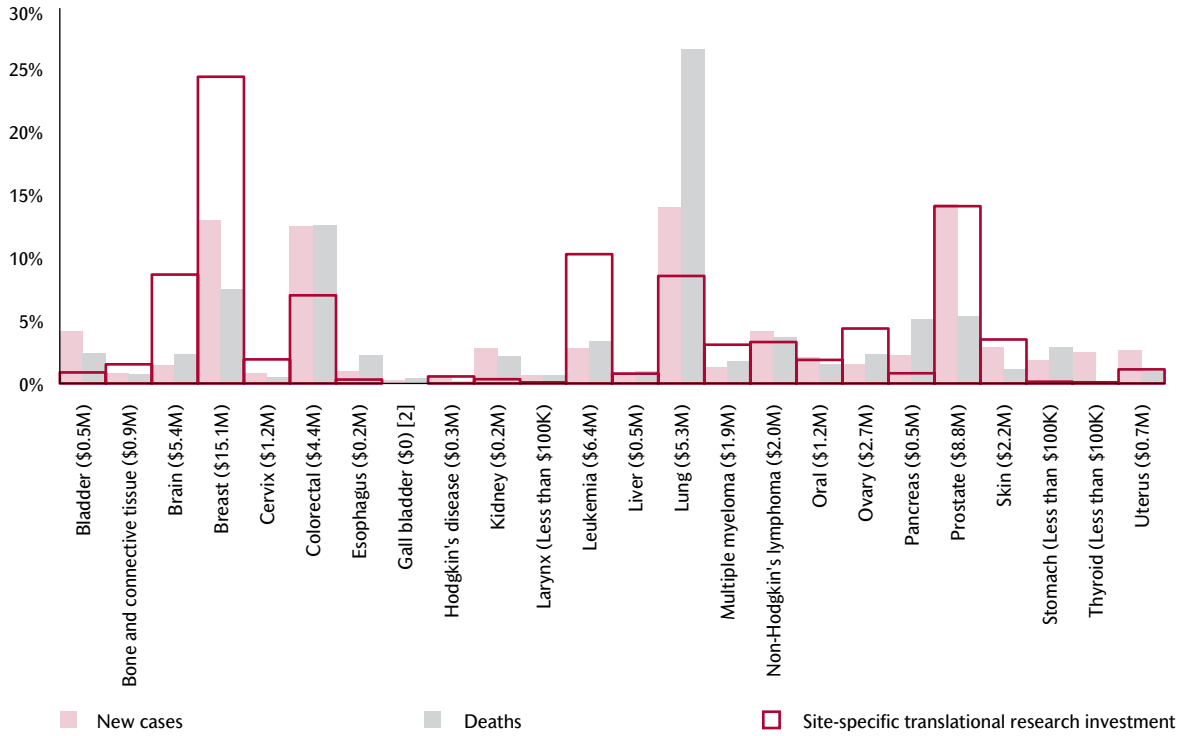
Site-specific translational research at an average of $62.1M per year accounted for 34.0% of the overall site-specific cancer research investment. Translational research with broadly based applicability (not specific to individual cancer sites) represented 38.9% of the translational research investment ($39.8M per year).

The average annual site-specific investment exceeded $5M per year for five cancer types: breast cancer ($15.1M), prostate cancer ($8.8M), leukemia ($6.4M), brain cancer ($5.4M), and lung cancer ($5.3M). With the exception of lung cancer, the first four cancer types also accounted for the largest proportions of the overall cancer research investment. Over half of the overall cancer research investment was translational for three cancer types: bladder cancer (66.8%), multiple myeloma (60.8%), and prostate cancer (52.0%).

Figure 3.4.1 compares the distribution of the site-specific investment in translational research with the distribution of new cancer cases and cancer deaths, proxy measures of the burden of disease. These data suggest that the translational research investment was disproportionately low relative to disease burden for many cancers, most strikingly for lung, colorectal, and pancreatic cancers, a finding that has been previously reported in the analysis of the overall cancer research investment.

FIGURE 3.4.1

DISTRIBUTION OF SITE-SPECIFIC TRANSLATIONAL CANCER RESEARCH INVESTMENT FOR 2005–2007 RELATIVE TO NEW CANCER CASES FOR 2006 AND CANCER DEATHS FOR 2005 [1]

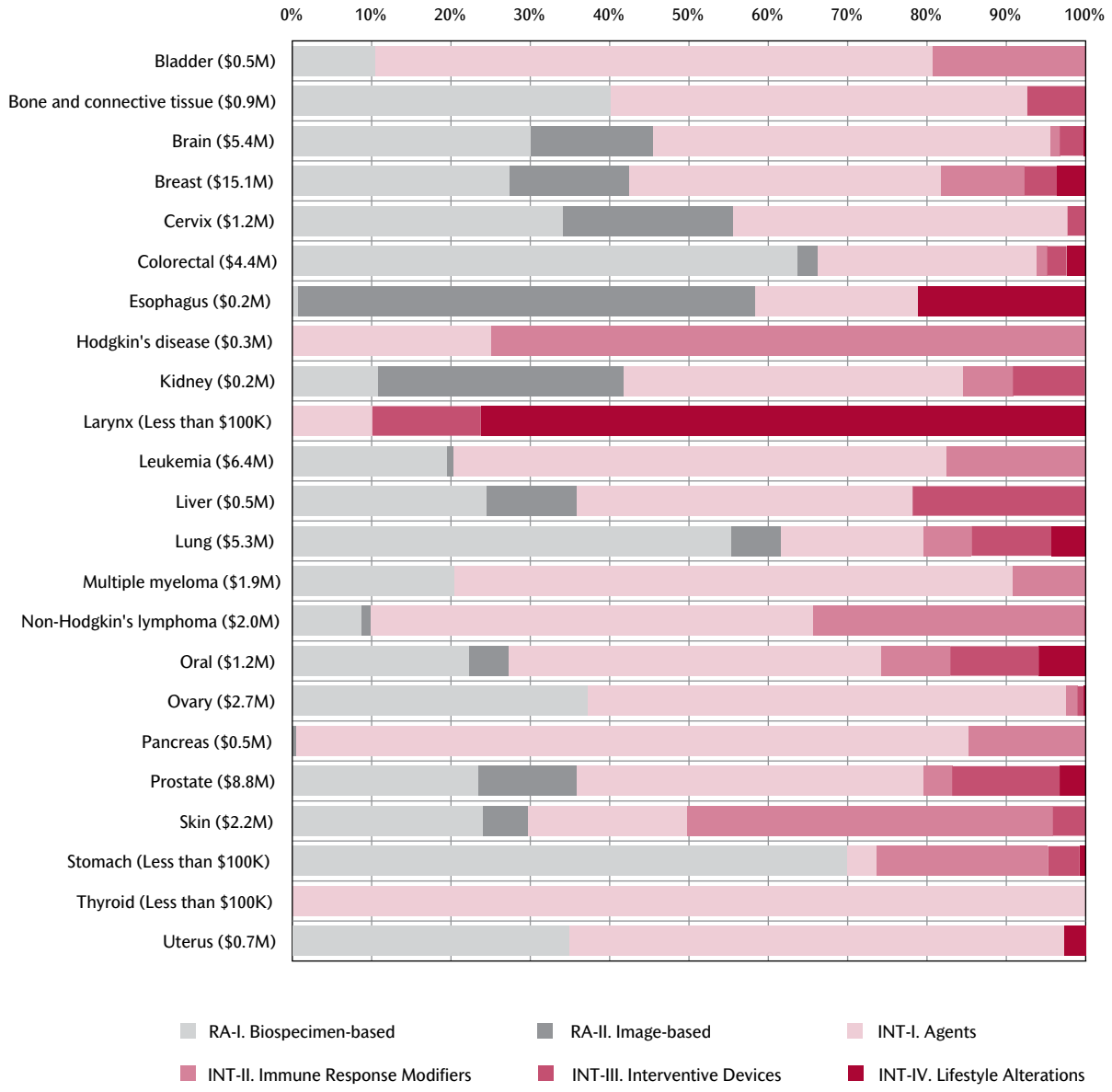


[1] Data on new cancer cases and cancer deaths are from: Canadian Cancer Society's Steering Committee. *Canadian Cancer Statistics 2010*. Toronto: Canadian Cancer Society, April 2010.
[2] There was no translational research focused on gall bladder cancer.

The distribution of the site-specific investments by the six modalities is shown in Figure 3.4.2. Agents accounted for the largest proportion of most site-specific investments (16 cancer sites). For stomach, colorectal and lung cancers, however, the largest proportions of the site-specific investments were for Biospecimen-based RA. For esophageal cancer, Image-based RA represented the largest proportion of the investment. The largest proportions of the investments for Hodgkin's disease and skin cancer were for Immune Response Modifiers.

FIGURE 3.4.2

DISTRIBUTION OF AVERAGE ANNUAL TRANSLATIONAL CANCER RESEARCH INVESTMENT BY MODALITY FOR INDIVIDUAL CANCER SITES, 2005–2007



The phase-specific investments for each cancer site are provided in Appendix E.

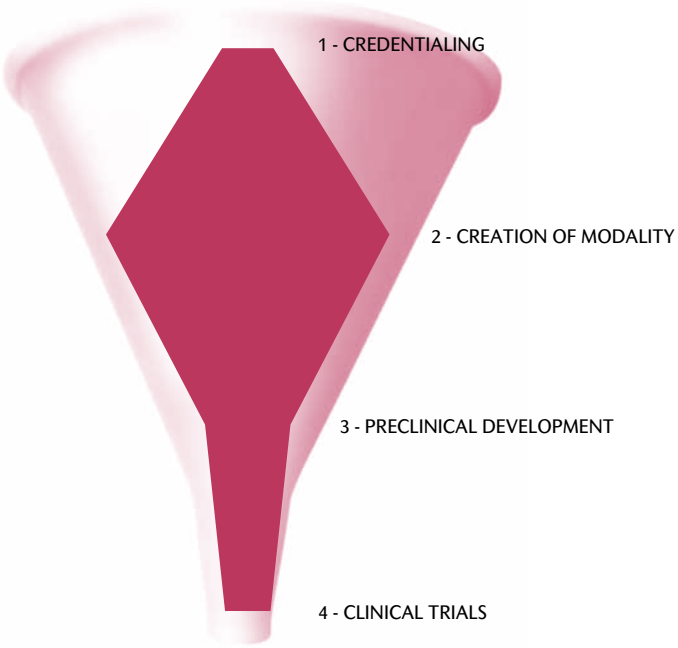
4. Summary

This report takes an in-depth look at early translational cancer research conducted in academic environments in the form of cancer research projects funded by major peer-reviewed programs offered by governments and charitable organizations in Canada. It likely represents between 33% and 41% of the overall early translational research environment, with industry being the key player particularly in the Clinical Trials phase.

Overall, the findings depict, in part, the classic "funnel" model of research translation—fewer research efforts progress through each successive translational phase (see Figure 4.1.1). In terms of the four phases of translation (Credentialing through Clinical Trials), nearly 40% of the investment was in the Creation of Modality phase, with investments in Preclinical Development and Clinical Trials research accounting for just 13% of the investment. What cannot be inferred from the data is whether there are barriers in the research funding environment that impede the progression of research to the early phase trials phase. Clearly, for translation to have its desired impact on cancer outcomes, understanding the barriers to clinical research, if any are in play, is critical.

FIGURE 4.1.1

DISTRIBUTION OF THE OVERALL EARLY TRANSLATIONAL RESEARCH INVESTMENT BY DEVELOPMENTAL PHASE



The findings do, however, suggest the following:

- Federal government organizations are key players in the early translational cancer research arena, not only in terms of direct support for research, but also in equipment/infrastructure support and capacity building. Increased harmonization of the strategic priorities around translational research by these organizations may help to facilitate sustained growth in this area.
- Strategic funding makes a difference. For example, the concentrated investment by the Ontario Institute for Cancer Research in translational research and supporting platforms has changed the research landscape in Ontario in just a few short years.

- Researchers engaged in translational research on Image-based RA and Interventive Devices received sizable investments in equipment/infrastructure from 2005 to 2007. Combined with the investments in Creation of Modality, some new technologies will come to fruition within the next few years.
- The low level of investment in Lifestyle Alterations is consistent with the CCRA report on investment in cancer risk and prevention research.[13] Compared with trials for drugs or other interventions, intervention studies designed to address behaviours or exposures are often complex, planning-intense, and rife with logistical, environmental, and financial hurdles. How best to support research on Lifestyle Alterations needs to be addressed.
- There are regional strengths in terms of translational research and capitalizing on these strengths may benefit the overall translational research effort. Although not a part of the analysis for this report, the extent to which Canadian cancer translational research relies on inter-institutional and multidisciplinary partnerships would be a very important area of future investigation. Consideration of outputs (e.g., material transfer agreements, filed patent applications, commercialized patents, new intellectual property, spin-off companies, etc.) as a means of assessing the impact of investment in translational research would also be an important exercise.

Several funding organizations have initiated new translational research initiatives in recent years. These include:

- The launch of The Terry Fox Research Institute in October 2007, with a mandate to support translational cancer research projects "with the potential to significantly improve the health of cancer patients"[14]
- The Pan-Canadian Cancer Biomarker Initiative, a collaboration between the Canadian Partnership Against Cancer and The Terry Fox Research Institute, identifies emerging technologies to improve early detection and treatment methods using biomarkers
- The Selective Therapies Target Identification Program, a joint initiative of The Terry Fox Research Institute and Ontario Institute for Cancer Research, focuses on new cancer target identification for the development of novel and selective anti-cancer therapeutics
- A special research competition on Predictive Oncology by the Canadian Breast Cancer Research Alliance/Canadian Breast Cancer Foundation initiative promotes research into the development of approaches to define and predict outcomes to specific treatments in specific subgroups of breast cancer patients based on molecular diagnostics and targeted therapies

13. As a general caveat, this report looked specifically at projects with a stated intention of cancer prevention and did not include studies that were more generally focused on chronic disease prevention.

14. See http://www.tfri.ca/about/.

- The Ontario Institute for Cancer Research Immuno- and Bio-therapies Program identifies new agents to selectively destroy cancer cells and minimize the adverse effects experienced by patients receiving treatments
- The Patient-Oriented Research Strategy of the Canadian Institutes of Health Research supports multidisciplinary research networks and the creation of accessible research units integrated into clinical or care settings, develops human capacity for patient-oriented research, and addresses systemic barriers

These investments will be captured in an upcoming report, which will document the patterns of cancer research investment over the five-year period of 2005 to 2009.

APPENDIX A.

LIST OF ABBREVIATIONS

CBCRA	Canadian Breast Cancer Research Alliance
CCRA	Canadian Cancer Research Alliance
CCRS	Canadian Cancer Research Survey
CSO	Common Scientific Outline
CTCRI	Canadian Tobacco Control Research Initiative
CTRNet	Canadian Tumour Repository Network
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
IND	Investigational New Drug
INT	Interventive
NCI	National Cancer Institute (U.S.)
PK/PD	Pharmacokinetics/Pharmacodynamics
PMPRB	Patented Medicine Prices Review Board
RA	Risk Assessment
TRWG	Translational Research Working Group

APPENDIX B.

TRANSLATIONAL RESEARCH INVESTMENT BY MODALITY AND PHASE, 2005–2007 [1] ($305.1M)

		RISK ASSESSMENT (RA)		INTERVENTIVE (INT)				
DEVELOPMENTAL PHASE	PARAMETER	I. Biospecimen-based	II. Image-based	I. Agents	II. Immune Response Modifiers	III. Interventive Devices	IV. Lifestyle Alterations	TOTAL
1 - CREDENTIALING	2005-07 amount	$21,459,661	$133,930	$8,324,035	$2,743,068	$3,568	$1,236,343	$33,900,606
	% overall translational investment	7.0%	0.0%	2.7%	0.9%	0.0%	0.4%	11.1%
	Project equivalents [2]	114.4	4.7	84.8	24.2	0.2	21.5	249.7
2 - CREATION OF MODALITY	2005-07 amount	$13,291,430	$15,776,890	$75,953,420	$11,869,723	$11,150,857	$1,096,706	$129,139,026
	% overall translational investment	4.4%	5.2%	24.9%	3.9%	3.7%	0.4%	42.3%
	Project equivalents [2]	65.3	139.2	567.4	97.3	120.6	9.1	998.8
3 - PRECLINICAL DEVELOPMENT	2005-07 amount	$7,011,540	$2,192,191	$10,333,127	$3,670,122	$1,526,636	$235,667	$24,969,283
	% overall translational investment	2.3%	0.7%	3.4%	1.2%	0.5%	0.1%	8.2%
	Project equivalents [2]	14.7	18.8	59.7	15.0	16.5	5.0	129.7
4 - CLINICAL TRIALS	2005-07 amount	$951,160	$546,623	$6,195,798	$3,368,128	$2,203,827	$1,766,207	$15,031,742
	% overall translational investment	0.3%	0.2%	2.0%	1.1%	0.7%	0.6%	4.9%
	Project equivalents [2]	2.5	5.3	127.9	21.0	38.9	15.3	210.9
SUPPORTING TOOLS	2005-07 amount	$15,715,204	$577,842	$7,785,002	$243,745	$498,358	$523,190	$25,343,341
	% overall translational investment	5.2%	0.2%	2.6%	0.1%	0.2%	0.2%	8.3%
	Project equivalents [2]	45.2	2.5	39.3	3.5	4.5	5.0	99.9
OTHER EQUIPMENT/ INFRASTRUCTURE	2005-07 amount	$8,374,225	$17,673,185	$30,981,563	$4,756,867	$13,987,468	$916,928	$76,690,236
	% overall translational investment	2.7%	5.8%	10.2%	1.6%	4.6%	0.3%	25.1%
	Project equivalents [2]	23.8	35.0	61.9	7.2	20.8	6.9	155.6
TOTAL	2005-07 amount	$66,803,220	$36,900,661	$139,572,944	$26,651,653	$29,370,714	$5,775,041	$305,074,234
	% overall translational investment	21.9%	12.1%	45.8%	8.7%	9.6%	1.9%	100.0%
	Project equivalents [2]	265.7	205.5	941.0	168.3	201.5	62.7	1,844.6

[1] The investments for all three years are shown.

[2] Project equivalents are a weighted counts of projects coded to modality-phase combinations. Not all projects are weighted as 100% translational and projects can be spread across more than one modality and phase.

APPENDIX C.

TRANSLATIONAL RESEARCH INVESTMENT BY PHASE AND ORGANIZATION, 2005–2007 [1] ($305.1M)

		DEVELOPMENTAL PHASE						
	FUNDING ORGANIZATION	1 - CREDENTIALING	2 - CREATION OF MODALITY	3 - PRECLINICAL DEVELOPMENT	4 - CLINICAL TRIALS	SUPPORTING TOOLS	OTHER EQUIPMENT/ INFRASTRUCTURE	TOTAL
FEDERAL GOVERNMENT ORGANIZATION/ PROGRAM	Canada Foundation for Innovation						$51,449,032	$51,449,032
	Canada Research Chairs Program	$6,667	$9,966,250		$750,000	$644,833		$11,367,750
	Canadian Institutes of Health Research	$8,961,484	$45,930,434	$9,918,312	$3,367,092	$2,971,267	$1,813,938	$72,962,528
	Genome Canada	$6,860,179	$3,745,618	$3,745,618		$8,686,461		$23,037,876
	Health Canada/Public Health Agency of Canada [2]	$289,015	$1,084,068	$413,678	$451,950	$223,081		$2,461,792
	National Research Council	$2,674,775	$2,292,487			$4,072,557		$9,039,818
	Natural Sciences and Engineering Research Council	$544,715	$7,559,138	$510,829		$381,867	$461,074	$9,457,623
	Networks of Centres of Excellence		$3,608,048	$15,000		$15,000		$3,638,048
	Social Sciences and Humanities Research Council				$40,384			$40,384
PROVINCIAL CANCER AGENCY	Alberta Cancer Foundation [3]	$843,075	$4,379,775	$1,196,935	$310,496	$1,419,383	$3,694,777	$11,844,441
	CancerCare Manitoba	$426,207	$550,656	$7,500	$7,500	$161,406		$1,153,268
	Cancer Care Nova Scotia	$5,000	$15,000	$5,000				$25,000
	Cancer Care Ontario				$90,000		$981,153	$1,071,153
	Saskatchewan Cancer Agency	$10,433	$15,000	$274,845				$300,277
PROVINCIAL HEALTH RESEARCH ORGANIZATION	Alberta Innovates – Health Solutions	$610,000	$1,678,099	$392,500	$62,092	$186,658	$20,955	$2,950,304
	Fonds de la recherche en santé du Québec	$1,020,612	$2,788,949	$322,150	$27,500			$4,159,211
	Manitoba Health Research Council	$118,238	$243,300	$17,850				$379,388
	Medical Research Fund of New Brunswick		$40,000					$40,000
	Michael Smith Foundation for Health Research	$454,379	$1,451,370			$238,299	$2,536,378	$4,680,425
	Nova Scotia Health Research Foundation		$316,232				$300	$316,532
	Ontario Institute for Cancer Research	$1,979,344	$8,356,490	$3,740,046	$3,634,798	$1,830,122	$8,666,169	$28,206,970
	Saskatchewan Health Research Foundation	$63,750	$272,393				$36,500	$372,643
VOLUNTARY ORGANIZATION	Brain Tumour Foundation of Canada	$25,000	$60,408		$49,285			$134,693
	C^{17} Research Network		$15,000		$25,000	$55,333		$95,333
	Canadian Association of Radiation Oncology	$22,618	$201,122	$57,076	$125,922	$6,660		$413,397
	Canadian Breast Cancer Foundation	$1,298,727	$3,426,702	$521,048	$913,741	$580,320		$6,740,538
	Canadian Cancer Society	$4,651,985	$14,365,763	$2,230,019	$3,136,951	$1,425,200	$4,122,414	$29,932,331
	Canary Foundation of Canada	$91,250				$642,750		$734,000
	Ovarian Cancer Canada						$21,860	$21,860
	Prostate Cancer Canada	$268,415	$1,299,527		$69,895	$185,000		$1,822,837
	The Cancer Research Society	$1,237,667	$2,833,967	$120,000	$20,000	$160,525		$4,372,158
	The Kidney Foundation of Canada	$111,680	$36,680					$148,359
	The Leukemia & Lymphoma Society of Canada	$136,000	$832,500	$25,000	$90,250	$5,000		$1,088,750
	The Terry Fox Foundation	$1,058,407	$11,282,724	$1,268,372	$1,654,020	$1,353,205	$2,883,030	$19,499,758
	Canadian Breast Cancer Research Alliance (funders not listed elsewhere)	$130,986	$491,329	$187,507	$204,866	$101,069		$1,115,757
	TOTAL	**$33,900,606**	**$129,139,026**	**$24,969,283**	**$15,031,742**	**$25,343,341**	**$76,690,236**	**$305,074,234**

[1] The investments for all three years are shown.

[2] Represents investment in the initiatives.

[3] In 2010 Alberta Cancer Foundation became the direct funding agency for funding programs administered by the former Alberta Cancer Board.

APPENDIX D.

TRANSLATIONAL RESEARCH INVESTMENT BY PHASE AND CITY [1], 2005–2007 [2] ($302.8M)

		DEVELOPMENTAL PHASE						
	CITY	1 - CREDENTIALING	2 - CREATION OF MODALITY	3 - PRECLINICAL DEVELOPMENT	4 - CLINICAL TRIALS	SUPPORTING TOOLS	OTHER EQUIPMENT/ INFRASTRUCTURE	TOTAL
Alta.	Calgary	$937,988	$2,279,642	$6,802,301	$52,832	$132,868	$286,724	$10,492,354
	Edmonton	$3,312,681	$3,754,637	$10,167,171	$1,042,742	$6,075,351	$1,418,631	$25,771,214
	Other			$13,958		$176,500		$190,458
	PROVINCIAL TOTAL	$4,250,669	$6,034,279	$16,983,431	$1,095,573	$6,384,720	$1,705,355	$36,454,026
B.C. [3]	Burnaby	$20,156	$140,848	$480,002				$641,006
	Vancouver	$20,457,301	$3,307,811	$22,646,048	$3,370,139	$720,780	$501,460	$51,003,540
	Other	$58,152	$125,614	$202,077	$285,558	$77,587		$748,988
	PROVINCIAL TOTAL	$20,535,609	$3,574,273	$23,328,128	$3,655,697	$798,368	$501,460	$52,393,534
Man.	Winnipeg	$2,183,809	$1,124,829	$3,049,541	$15,000	$136,418	$97,983	$6,607,579
N.B.	PROVINCIAL TOTAL			$140,085	$3,437		$47,046	$190,568
N.L.	St. John's	$138,774		$130,850	$5,000	$29,184		$303,808
N.S.	Halifax	$35,561	$173,916	$2,367,508	$359,849	$3,874		$2,940,708
	Other			$276,202				$276,202
	PROVINCIAL TOTAL	$35,561	$173,916	$2,643,710	$359,849	$3,874		$3,216,910
Ont.	Guelph			$1,732,521	$144,488		$8,750	$1,885,758
	Hamilton	$1,989,698	$577,798	$7,205,703	$3,511,667	$726,971		$14,011,836
	Kingston	$359,681		$11,277,088	$192,676	$272,074	$271,405	$12,372,923
	London	$705,121	$3,503,431	$1,613,975	$29,145	$1,853,008	$37,030	$7,741,709
	Ottawa	$2,804,212	$31,667	$6,221,470	$421,097	$990,332		$10,468,777
	Sudbury	$31,815	$88,361	$312,741			$34,976	$467,894
	Toronto	$27,348,089	$16,349,087	$27,986,443	$8,047,427	$11,523,026	$1,956,682	$93,210,754
	Waterloo			$798,295		$307,738	$224,941	$1,330,973
	Other	$55,000	$5,775	$25,750		$7,374	$10,000	$103,899
	PROVINCIAL TOTAL	$33,293,615	$20,556,118	$57,173,984	$12,346,500	$15,680,523	$2,543,783	$141,594,523
P.E.I.	Charlottetown			$60,000		$26,363	$102,000	$188,363
Que.	Montréal	$4,820,735	$274,958	$27,909,211	$7,411,993	$2,599,144	$528,888	$43,544,928
	Québec	$1,003,229	$484,723	$2,899,348	$400,948	$697,874	$20,000	$5,506,122
	Sherbrooke	$30,862	$2,549,797	$2,089,241		$1,404,272		$6,074,172
	Trois-Rivières			$814,078			$34,800	$848,878
	Other	$90,293		$18,250	$41,844		$4,561	$154,947
	PROVINCIAL TOTAL	$5,945,119	$3,309,477	$33,730,127	$7,854,785	$4,701,289	$588,248	$56,129,046
Sask.	Saskatoon	$360,064	$1,999,714	$1,006,845	$760,473	$1,522,475	$63,750	$5,713,321
	Other			$8,374				$8,374
	PROVINCIAL TOTAL	$360,064	$1,999,714	$1,015,219	$760,473	$1,522,475	$63,750	$5,721,696
	TOTAL	**$66,743,220**	**$36,772,606**	**$138,255,074**	**$26,096,314**	**$29,283,214**	**$5,649,624**	**$302,800,053**

[1] The location of the nominated principal investigator's institution is used to assign investment to specific cities. Excludes awards to trainees who were at institutions outside Canada.

[2] The investments for all three years are shown.

[3] BC Cancer Agency data are not included and figures may underestimate the investment in B.C.

APPENDIX E.

TRANSLATIONAL RESEARCH INVESTMENT BY PHASE AND CANCER SITE, 2005–2007 [1] ($305.1M)

	DEVELOPMENTAL PHASE						
CANCER SITE	1 - CREDENTIALING	2 - CREATION OF MODALITY	3 - PRECLINICAL DEVELOPMENT	4 - CLINICAL TRIALS	SUPPORTING TOOLS	OTHER EQUIPMENT/ INFRASTRUCTURE	TOTAL
Bladder	$205,766	$1,271,738	$62,569	$51,511	$9,833	$30,483	$1,631,901
Bone and connective tissue	$475,430	$917,350	$154,922	$208,363	$939,788	$138,520	$2,834,373
Brain	$1,391,069	$8,131,701	$1,338,491	$458,601	$2,546,286	$2,268,591	$16,134,737
Breast	$7,178,301	$22,965,179	$5,044,423	$3,470,907	$4,766,223	$2,030,601	$45,455,634
Cervix	$418,366	$1,286,585	$366,822	$445,290	$440,148	$606,466	$3,563,677
Colorectal	$3,011,212	$3,700,092	$1,457,866	$412,384	$4,359,137	$117,832	$13,058,523
Esophagus	$28,185	$337,553	$59,270	$23,178	$9,119	$117,260	$574,566
Hodgkin's disease		$767,374	$85,468	$25,625		$158,330	$1,036,797
Kidney	$196,512	$180,157	$45,098	$79,106		$127,225	$628,099
Larynx	$23,967	$80,139		$23,178	$9,119	$22,406	$158,809
Leukemia	$1,040,334	$12,824,615	$2,260,378	$1,758,325	$789,584	$483,169	$19,156,406
Liver		$915,487	$143,293	$165,319	$120,525	$108,609	$1,453,233
Lung	$7,899,711	$4,750,965	$1,307,200	$760,399	$288,676	$919,659	$15,926,610
Multiple myeloma	$689,221	$1,653,552	$812,704	$1,260,721	$543,241	$779,160	$5,738,600
Non-Hodgkin's lymphoma	$553,934	$2,807,060	$1,245,940	$833,192	$204,614	$489,744	$6,134,484
Oral	$499,543	$1,230,657	$593,932	$499,421	$246,561	$417,689	$3,487,804
Ovary	$2,463,044	$2,800,907	$1,166,634	$74,356	$1,234,447	$400,087	$8,139,475
Pancreas	$133,333	$902,892	$153,511	$81,667	$29,167	$206,113	$1,506,682
Prostate	$2,297,697	$10,305,594	$2,676,061	$2,541,547	$711,083	$7,739,375	$26,271,357
Skin	$333,982	$3,733,506	$2,093,068	$74,681	$49,703	$228,749	$6,513,690
Stomach	$109,501	$151,200					$260,701
Thyroid		$93,150		$60,000		$17,647	$170,797
Uterus	$125,785	$1,091,944	$149,570	$211,921	$186,513	$320,062	$2,085,794
Other Sites	$386,428	$3,469,951		$304,589	$55,333	$220,859	$4,437,161
Non-specific/All Sites	$4,439,283	$42,769,677	$3,752,061	$1,207,462	$7,804,242	$58,741,601	$118,714,326
TOTAL	**$33,900,606**	**$129,139,026**	**$24,969,283**	**$15,031,742**	**$25,343,341**	**$76,690,236**	**$305,074,234**

[1] The investments for all three years are shown.

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