CRITICAL PATH FOR IDEA AWARDS

Purpose: The point of asking for the "critical path" is to have the PI place the project on a research continuum (i.e., temporal trajectory) that begins with an idea or hypothesis and continues through development leading to a defined result of practical value (e.g., in the clinic or community). First, ask yourself the question: How will my project and its research goals/milestones lead to a measurable impact on the prevention, detection, diagnosis and treatment, reduction in community and social burden, or improved patient quality of life for breast cancer?

Background: Breast cancer research funding has been successful in the creation of new knowledge. However, the useful application of this knowledge to prevent and detect the disease, and increase survival and quality of life for breast cancer patients could be improved. If funding agencies and researchers are to be accountable to stakeholders, more emphasis needs to be placed on the "critical path" from research-to-practice.

In 2003 Best et al. (*Cancer Epidemiology Biomarkers & Prevention*,12:705-712) distinguished two pathways to practical application of research, "….. it is important to view "translational research" to encompass not only the pervasive view of transfer of basic science discoveries into clinical applications ("bench to bedside"), but also its transfer into effective interventions at the population level with active community participation in the process ("bench to trench"). Collaboration between research producers and research consumers in this translational approach is critical to reduce the cancer burden at the population level, the ultimate measure of benefit to all people."

An early conceptualization and model for a "critical path" between research and action, developed in the context of smoking/tobacco, was advanced in 1985 by Peter Greenwald and Joseph Cullen (*J. Natl. Cancer Inst*., 74:543-551) who distinguished phases of cancer control research:

Basic Research & Epidemiology
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Phase I: Hypothesis development
Phase II: Methods development
Phase III: Controlled intervention trials
Phase IV: Defined population studies
Phase V: Demonstration and implementation
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Nationwide prevention and health services programs

In addition, Phases I-V incorporate "feedback loops", so new hypotheses and methods can be generated in concert with novel intervention efforts. The "take home message" from this model is that the CBCRP expects researchers to actively consider where and how their results might find practical applications at the end of the "critical path." Thus, your research decision

making and innovative approach should incorporate these elements when planning projects: (i) an awareness of the social (i.e., human and community) needs and environmental determinants of health and disease, (ii) limitations of current prevention, detection, prognosis, and treatment strategies, (iii) the state of the existing science for the topic being addressed, (iv) an understanding of the limitations and barriers that block translation to a higher level, and (v) a framework for visualizing the desired research outcome and potential benefit (practical uses).
Overview and conceptual framework: The CBCRP believes that each grant should be capable of advancing the topic under investigation along the "critical path." To provide an outline to get you started, we have developed the following chart, which derived and greatly expanded from Table 1 in the FDA's "Challenge and Opportunity on the Critical Path to New Medical Products" (http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html). For the "critical path" dimensions/levels we have added definitions and provided examples of activities relevant to both the "basic science/clinical" and the "public health/community/population/social science" disciplines.

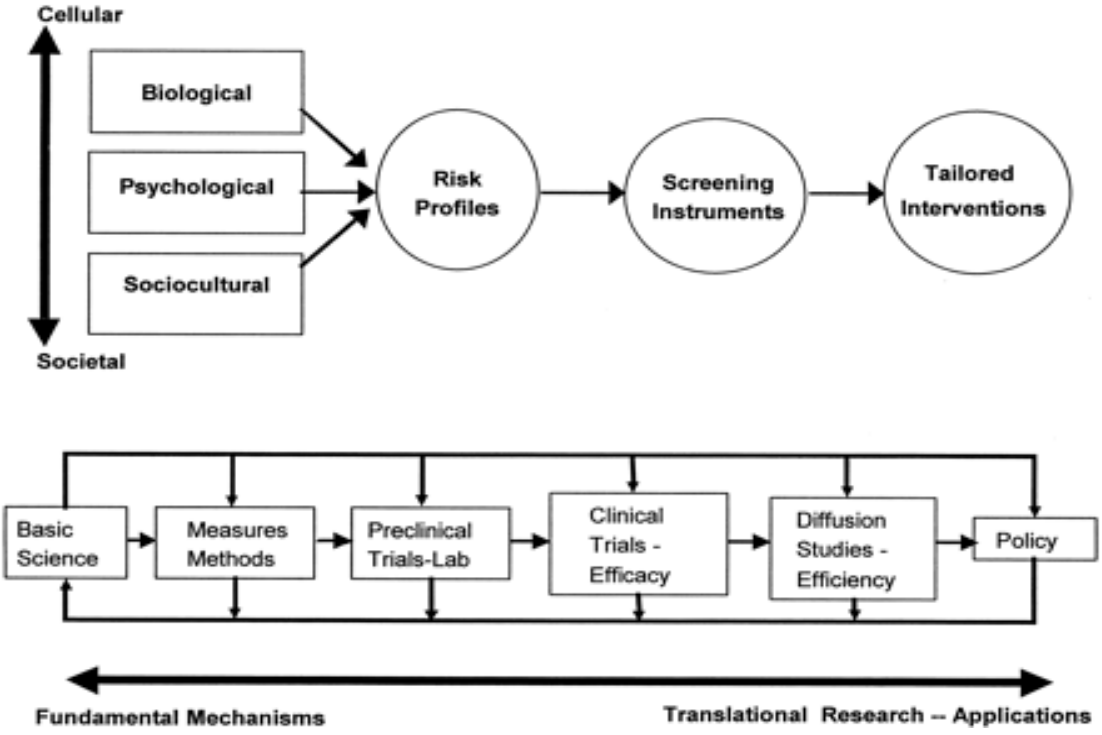
Dimension/Level	Definitions	Examples of activities
Concept & hypothesis development	Discovery and exploration The links between the hypothesis and a research problem in breast cancer Considering problems from novel perspectives Initial tests in basic systems Establishing the basis for scientist-community interactions	Basic science/clinical track: o Assessing background information in breast cancer, other cancer types, and cell/biological models. o Developing new information on breast cancer through data collection. o Establishing relationships to breast cancer. o "Mining" basic science for new treatment, detection, and prognosis concepts. o Pilot testing of new compounds and detection/prognosis strategies. Community/population/intervention track: o Considering social needs, disparities, and community issues from new perspectives. o "Mining" basic science for new epidemiological, behavioral, psychological, sociocultural or policy concepts. o Conceptualizing possible interventions. o Planning culturally appropriate, acceptable, and feasible delivery approaches for new community-based interventions and prevention strategies. o Identifying target populations and establishing new collaborations. o Demonstrating or gaining trust and acceptance by the community. o Pilot data collection and field methodology

Dimension/Level	Definitions	Examples of activities
		developed. (Cancer control phase I --Cullen & Greenwald model)
Methods development and establishing "proof-of-principle"	Obtaining significant data to substantially support the hypothesis and point the direction for future work Establishing direct relevance to breast cancer in the basic science, clinical, or community settings Active scientist-community "partnering" in the research "Multi-disciplinary" collaborations (researchers in different disciplines work <u>independently</u> or sequentially on a common problem) Testing in small populations & initial data gathering	<u>Basic science/clinical track:</u> o Studies in model systems. o Integration into and challenging existing information on breast cancer. Publication. o Early pre-clinical phases (e.g., rational drug design, validate lead compounds). o Showing the potential to challenge and improve upon existing therapies and detection/prognosis standards. <u>Community/population/intervention track</u>: o Refine prevention strategies and collaborative networks. o Preliminary field tests of epidemiological hypotheses, policies or intervention methods and delivery systems. o Determination of outcome and process variables. o Development of measurement tools and data collection procedures. [Cancer Control Phases II and III (small trials) — Cullen & Greenwald model]
Developmental and testing phase	Formulating a strategy for practical application Stimulate interest in other researchers and "interdisciplinary" collaborations (researchers working <u>jointly</u> to address a common problem) Generation of derivative concepts (feedback loop)	<u>Basic science/clinical track:</u> o Significant findings showing a clear connection to the disease. o Formulation and testing in animal models. o Publication and dissemination. o Late pre-clinical studies and early (Phase I & II) clinical trials. o Analysis of target groups and cost effectiveness. o Definitive links to target populations for detection, prognosis, treatment strategy. <u>Community/population/intervention track</u>: o Larger scale testing of epidemiological

Dimension/Level	Definitions	Examples of activities
	Demonstrating efficacy or utility in a human detection, prognosis, or therapeutic setting. Researchers and community groups "partner" and reach common goals	hypotheses, policies, or interventions in a well-defined populations enabling generalization to ultimate target populations (efficacy trial). o Systematic testing of epidemiological hypotheses, policy proposals, or community-based intervention in a larger population under "real-world" conditions (effectiveness trial). o Publication and dissemination. [Cancer Control Phases III (larger trials) & IV—Cullen & Greenwald model]
Implementation & translation	Wide acceptance of concept Improvements for detection, diagnosis, prognosis, and treatment Tangible social benefit New public health policies evolve from community-driven needs and researcher-driven outcomes to decrease disparities in detection, treatment, and disease burden Prevention and lowering risk for breast cancer	Basic science/clinical track: o Final basic research studies to validate a new clinical approach. o Feedback loop to stimulate new concepts to be tested (level #1) o Phase III & IV clinical trials. o Application of new therapies and chemoprevention approaches. o Advancing the standard of care. Community/population/intervention track: o Demonstration and implementation on a large scale. o Diffusion studies to other populations and communities. o Integration into cancer control health policy. o Interventions to lower disease incidence and mortality. (Cancer Control Phase V—Cullen & Greenwald model)

Finally, a major "critical path" limitation is the absence of cross-talk between disciplines. "Basic/clinical" and "public health/social/population/community" researchers often work apart. Thus, the CBCRP is asking researchers to consider and explore avenues of research communication and common interest that allow the different disciplines to become integrated and lead to practical applications directed at breast cancer. This approach was recently presented by Best et al. (*Cancer Epidemiology Biomarkers & Prevention*,12:705-712),who proposed the term "transdisciplinary research." "*Transdisciplinarity* is a process by which researchers work jointly using a shared conceptual framework that draws together discipline-

specific theories into a new synthesis of concepts, methods, measures, and approaches to address a common problem."



Final thoughts: Provide a brief, thoughtful discussion of how your research project would advance along a "critical path" to take your topic from one level to the next and provide practical applications. How might your innovative research "make a significant difference" and provide "transdisciplinary links" between the basic science, clinical, and public health/social/population/community research landscapes?