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Impact of Aging on Animal Models of Disease

The rationale for this concept was developed as a result of a scientific Summit which explored the role of aging biology in the etiologies of chronic diseases.

Advances in Geroscience: Impact on Healthspan and Chronic Disease

October 30th – November 1st, 2013

RFA Concept Proposal
March 11th, 2015
Kevin Howcroft, DCB

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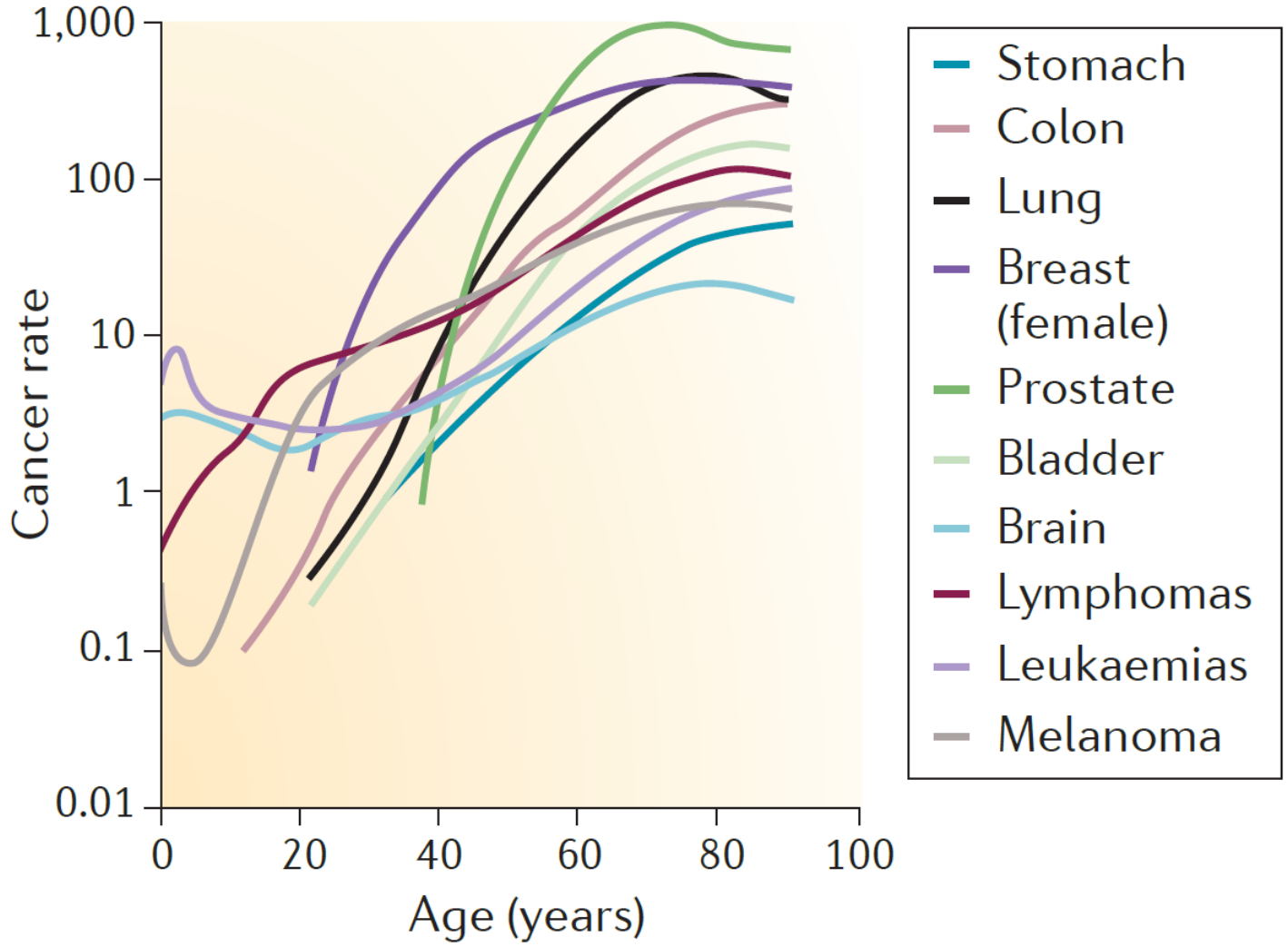
The Incidence of Most Human Cancers Increases with Age



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Mouse Models Used to Study Cancer Processes or Response to Therapy…

Treatment
- Preclinical development of novel targeted therapies in genetically defined tumors

Drug Resistance
- Enhance understanding of primary drug resistance
- Elucidate mechanisms of acquired resistance to drugs

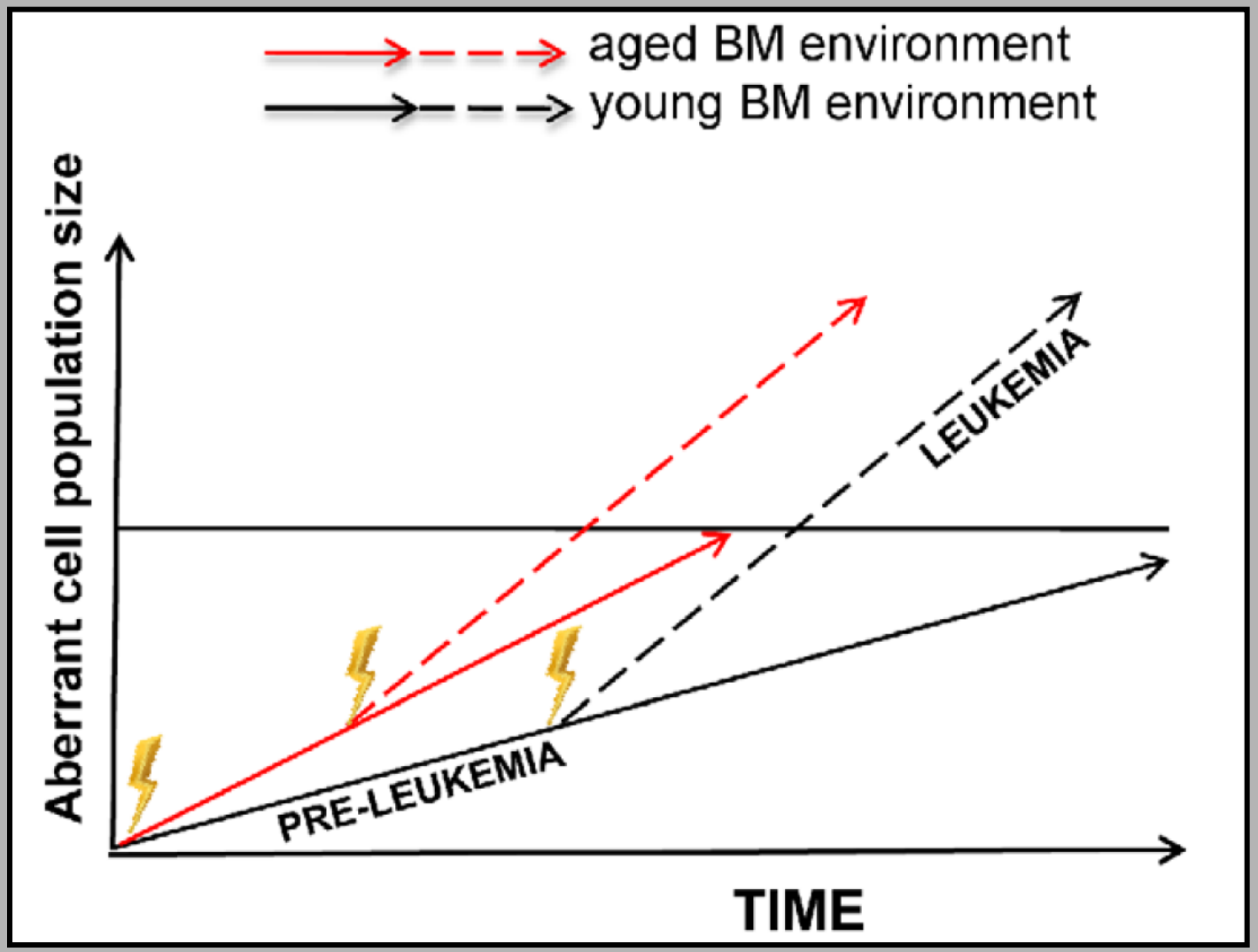
Cancer Prevention
- Test the effectiveness of agents to prevent cancer formation/ progression
- Establish the effect of environmental changes on tumor burden in mice genetically modified to develop specific cancer types

Early Detection
- Identification of potential screening biomarkers
- Development of molecular imaging strategies

Metastasis
- Identification of genetic determinants of metastatic progression
- Development of strategies to interfere with metastasis formation

Katerina Politi and William Pao
J Clin Oncol 29:2273-2281

Acute Myeloid Leukemia Progression is Accelerated in Aged Mice



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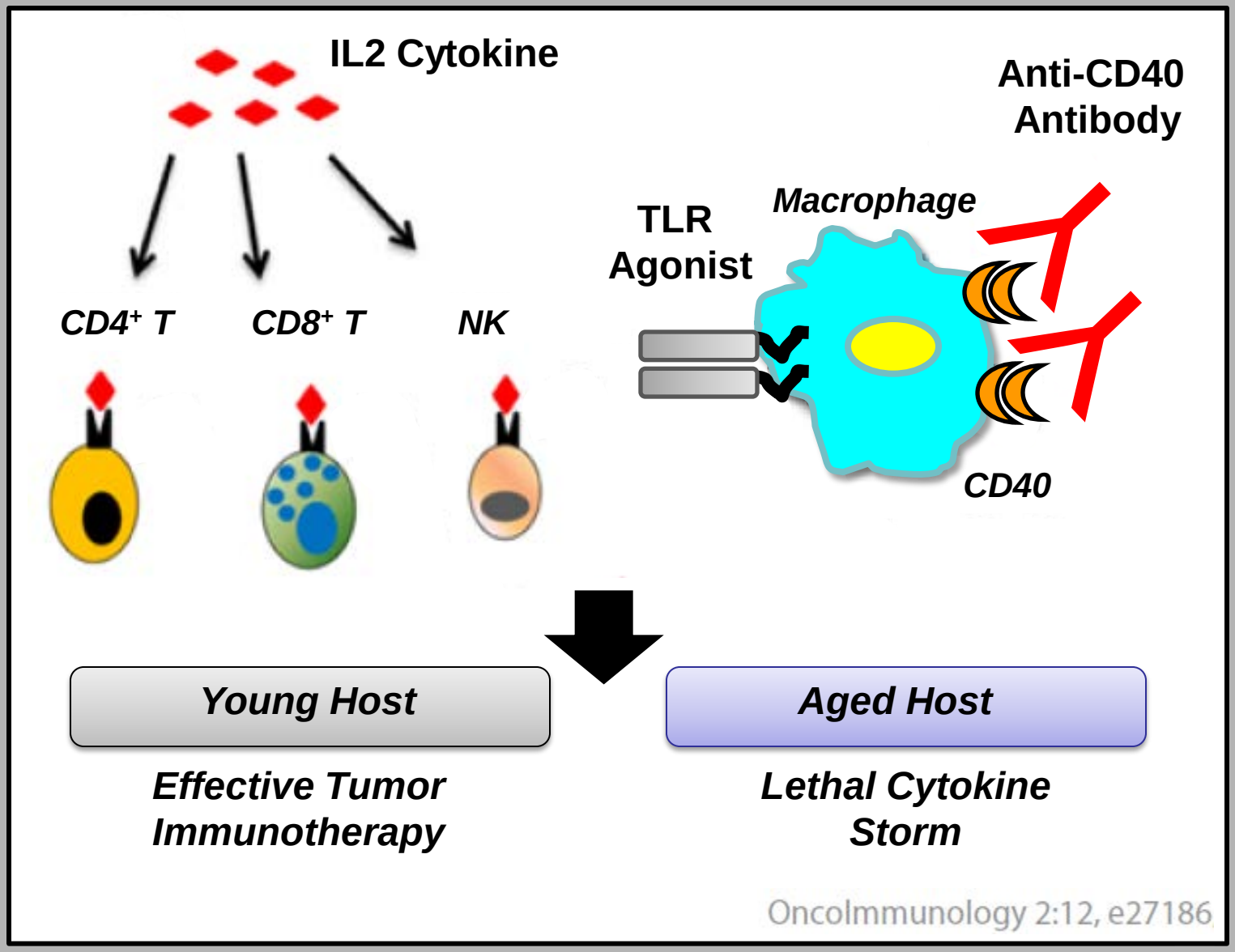
Aging Prediposes to Acute Inflammatory Pathology Following Tumor Immunotherapy



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Barriers to Progress

- o animal care costs to generate a colony of aged mice;
- o specialized expertise is required to conduct research using aged animals.
- o experiments to generate data for publication or grant renewal takes longer; and
- o higher burden on laboratory personnel to dedicate time to these projects.

Nevertheless, studies involving older animals may be critical to advancing basic research and translational studies from animal models to human populations.

Initiative Goal

Use existing, well-characterized, inducible mouse models of human cancer to determine whether the age of the animal when the cancer is induced is a critical factor in assessing whether the:

- pathobiology of the cancer
- response to intervention

better predicts the human condition.

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Proposed Implementation Plan
Mechanism

Mechanism: UH2/UH3 Cooperative Agreement

UH2 phase (years 1-2)

Milestones:

- Generate aged cohorts
- Pilot experiments to assess feasibility
- **Proposed budget capped at $150,000 TC/2years**

UH3 phase (years 3-5)

Milestones:

- Characterize the cancer phenotype or response to intervention in older animals compared to the established phenotype in younger aged animals
- **Proposed budget capped at $450,000 TC/3years**

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Proposed Implementation Plan
Funding Opportunity

Request to participate on an **RFA** with other NIH Institutes including NIA, NIAID, NIDCR, NIEHS, and NIMH

- **NIA is the lead Institute and proposes to co-fund**
  - **Two awards at 50%**

Proposed Set Aside for 01 Year (FY16):

- 6 awards: up to $250,000 DC/$375,000 TC

Estimated Cost for Total Project Period:

- 6 awards: $2,000,000 DC/$3,000,000 TC

Portfolio Analysis:

No grants examining induction of cancer in aged mouse models were identified – indicating this is an understudied research area.

Fulfilling the Goals of the RFA is Expected to Generate:

- **Research Community:** Will meet to review progress and share information.
- **Resource:** Establish biological and technical guideposts to assess cancer progression or response to therapy in aged animals.
- **Validation Data Set:** Test the hypothesis that age of the animal is a critical factor in generating an accurate depiction of human cancer progression or response to intervention.

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Questions?