PAR EBV, NHL, & HD

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Thank you to the BSA Reviewers for their helpful and thoughtful suggestions

Their suggestions have been incorporated into the slides or will be verbally expressed during the oral presentation.

PAR Purpose

- Focus on the role of EBV infection on Non-Hodgkin Lymphoma (NHL) and Hodgkin disease (HD) development with or without an underlying HIV infection and AIDS.
  - Increase our understanding through mechanistic, epidemiological, or translational studies that examine how EBV promotes NHL or HD initiation, progression, and the resulting disease sequelae.
  - Provide insights into mechanistic differences of EBV infection and lymphomagenesis between HIV+ and HIV- persons.

Background: NHL and EBV & HIV positive

- Aggressive B cell lymphomas are
  - an AIDS-defining cancer when it occurs in a person living with HIV (PLWH)
  - ~ 40% of EBV positive U.S. NHL cases develop in PLWH
  - Most prevalent EBV-positive NHL types
    - DLBCL (diffuse large B cell lymphoma)
    - BL (Burkitt lymphoma)
    - CNS-NHL (central nervous system NHL)*
  - Despite treatment PLWH remain at an elevated risk for EBV positive NHL

* 100% EBV positive

Background: NHL and EBV positive

- EBV positive NHL differs in HIV negative persons
  - Approximately 50% of NHL-T cell and 13 % of NHL-B cell lymphomas are EBV positive
    - DLBCL is not EBV positive
    - Few CNS lymphomas are EBV positive
  - Age of Onset
    - Range 64-74 years, median age 67

Background: HD and EBV & HIV positive

- Mixed cellularity
- Reed-Sternberg Cells generally EBV infected
- Unique features of the Tumor Microenvironment

Background: HD and EBV positive

- EBV positive HD differ in HIV negative persons
  - More frequent B symptoms
  - Age of Onset

Research Suggestions:
NHL or HD and EBV in HIV+ and/or HIV- Patients

- How does HIV direct, either alone or in association with EBV, **establishment of an environment** for the development of NHL or HD;
- How and why does **HIV infection and EBV reactivation have an impact on responses to treatment** that differ from HIV-negative NHL or HD patients;
- Are there **population differences** in the development of NHL or HD;
- Do **exogenous or endogenous environmental factors contribute** to NHL or HD in persons co-infected with HIV and EBV?

Research Suggestions: Role of EBV in NHL or HD

- **Mechanistic studies** exploring how EBV infection causes NHL or HD;
- Explore how and why **different EBV latency programs** are selected by sub-types of NHL or HD;
- Examine how **endogenous factors** affect the development of NHL or HD;
- Explore **population and sex differences** in the development and responses to therapy of NHL or HD;
- Develop **cell, tissue, or small animal models** to study EBV and NHL or HD; and
- Develop **preventive and/or therapeutic strategies** for EBV-related NHL or HD

Justification for Use of a PAR

- A necessary mechanism to incentivize investigators to propose high risk projects to address NHL with and without an HIV infection.
- Endorsed by the BSA Ad hoc Subcommittee on HIV and AIDS malignancy.
- Applications will be reviewed by a panel of area experts convened by NCI DEA.
  - Expertise in a variety of disciplines is required to review the entire group of applications received per receipt date in a single review meeting.

Administrative

- Mechanisms
  - R01 (5 yrs.)
  - R21 (2 yrs.)
- Anticipate Funding
  3-4 R01s and 3-4 R21s
- Receipt Dates
  - NCI-DEA specific receipt date **one per year** for **all applications** for 3 years
  - ~ Aug. 2021, 2022, & 2023

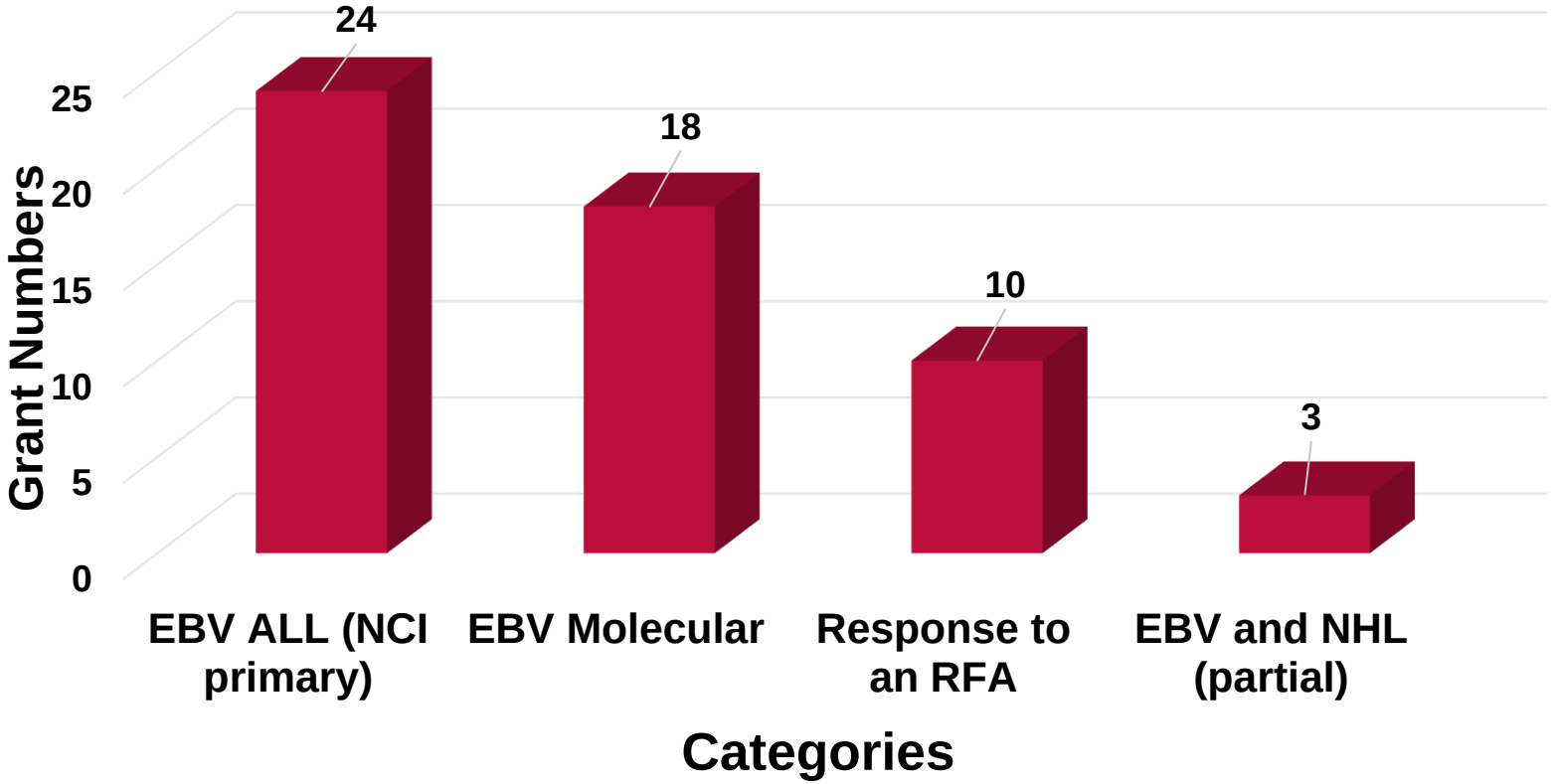
Budget

- Source of Funds RPG
- First Year Budget Total
  - $ 2M per year

  (cost sharing between NCI AIDS funds & non-AIDS funds approved by OAR)
- Total Budget for Project Period
  - ~$ 18M total

  (3 receipt dates for up to 5 years)

NCI Portfolio Analysis FY20 and FY21



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