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Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases

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Credit: NIAID

Chief, Neuroimmunological Diseases Section

Contact Information

Bibi Bielekova, M.D. ⤤ (link is external)(https://ned.nih.gov/search/ViewDetails.aspx?NIHID=0010013292)

Major Areas of Research

- Development of combinatorial biomarkers for reliable measurement of pathophysiological processes (e.g., inflammation, neurodegeneration) in patients with immune-mediated diseases of the central nervous system, especially multiple sclerosis (MS)
- Validation of MS disease mechanisms and therapeutic targets within the context of interventional clinical trials and longitudinal follow-up of patients on FDA-approved disease-modifying treatments
- Identification of biomarker signatures that can predict a drug's efficacy on clinical outcomes and development of algorithms that optimize therapeutic selections by combining patients' pre-treatment cerebrospinal fluid (CSF) biomarker profiles with newly acquired knowledge of the drug's intrathecal effects as measured by CSF biomarkers

Program Description

The mission of the Neuroimmunological Diseases Section is to understand, diagnose, prognosticate, and cure neuroimmunological diseases.

Clinical research workflow at Neuroimmunological Diseases Section

Credit: NIAID

Through understanding of the mechanisms that participate in central nervous system (CNS) injury and those that have neuroprotective functions, we aim to develop effective therapies for neuroimmunological diseases. Because observational studies cannot determine causal relationships, we use proof-of-principle interventional trials supported by biomarker/mechanistic studies and mathematical modeling to investigate major hypotheses about the pathophysiology of MS.

Our studies revealed that relapsing-remitting MS (RRMS) and progressive MS are categorical descriptions of early versus evolved stages of the identical continuous disease process characterized by aberrant activation of adaptive immunity that targets CNS tissue, which evolves by progressive intrathecal compartmentalization and terminal differentiation of T and B cells to a treatment-resistant stage. The multiplicity of potential pathogenic processes in evolved MS makes it unlikely that a single therapeutic agent will have major clinical efficacy. Analogous to cardiovascular diseases, effective therapy will require combinations of therapeutics that target patient-specific drivers of disability. We believe that the development of such combination treatments requires the ability to reliably measure the diverse CNS pathophysiological processes in living people and thereby define process-specific biomarkers to use as outcomes in Phase II trials. Indeed, using CSF biomarkers and systems biology methodology we have defined (and validated in an independent cohort) molecular signature(s) that differentiate MS from other CNS

diseases and those that can reliably measure the levels of intrathecally compartmentalized inflammation and CNS tissue destruction. Our goal is to formulate (and validate) a framework where a combinatorial CSF biomarker(s) can provide reliable diagnostic, prognostic, and therapeutically predictive information that will empower neurologists to practice precision medicine.

Biography

Dr. Bielekova received an M.D. in 1993 from Comenius University in Bratislava, Slovakia. After a medical internship at SUNY Downstate Medical Center in Brooklyn and a neurology residency at Boston University, she did a 3-year postdoctoral research fellowship at the NINDS Neuroimmunology Branch (NIB). She remained at NIB for an additional 5 years as a staff physician, focusing on development of novel therapies for MS. In 2005, she became associate professor of neurology with tenure and director of the Waddell Center for MS at University of Cincinnati. In 2008, she moved back to NINDS as an investigator. In 2018, Dr. Bielekova transferred as a senior investigator to NIAID. Her laboratory is studying mechanisms of immunoregulation and immune-mediated CNS tissue injury in MS and other neuroimmunological diseases with a long-term goal of developing effective therapies. In addition, Dr. Bielekova is a principal investigator on several innovative protocols including adaptively designed Phase I/II clinical trials.

Research Group

Lab

Chris Barbour

Paavali Hannikainen

Kayla Jackson

Peter Kosa

Raj Masvekar

Linh Pham

Jon Phillips

Elena Romm

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Clinical

Tiffany Hauser

Mary Sandford

Alison Wichman

Michelle Woodland

Selected Publications

Kosa P, Barbour C, Wichman A, Sandford M, Greenwood M, Bielekova B. NeurEx: digitalized neurological examination offers a novel high-resolution disability scale. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/30349859) *Ann Clin Transl Neurol*. 2018 Sep 24;5(10):1241-1249.

Weideman AM, Tapia-Maltos MA, Johnson K, Greenwood M, Bielekova B. Meta-analysis of the Age-Dependent Efficacy of Multiple Sclerosis Treatments. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/29176956) *Front Neurol*. 2017 Nov 10;8:577.

Barbour C, Kosa P, Komori M, Tanigawa M, Masvekar R, Wu T, Johnson K, Douvaras P, Fossati V, Herbst R, Wang Y, Tan K, Greenwood M, Bielekova B. Molecular-based diagnosis of multiple sclerosis and its progressive stage. ☐ (link is external)(https://www.ncbi.nlm.nih.gov/pubmed/29059494) *Ann Neurol*. 2017 Nov;82(5):795-812.

Natrajan MS, de la Fuente AG, Crawford AH, Linehan E, Nuñez V, Johnson KR, Wu T, Fitzgerald DC, Ricote M, Bielekova B, Franklin RJ. Retinoid X receptor activation reverses age-related deficiencies in myelin debris phagocytosis and remyelination. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/26463675) *Brain*. 2015 Dec;138(Pt 12):3581-97.

Komori M, Blake A, Greenwood M, Lin YC, Kosa P, Ghazali D, Winokur P, Natrajan M, Wuest SC, Romm E, Panackal AA, Williamson PR, Wu T, Bielekova B. Cerebrospinal fluid markers reveal intrathecal inflammation in progressive multiple sclerosis. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/25808056) *Ann Neurol*. 2015 Jul;78(1):3-20.

Wuest SC, Edwan JH, Martin JF, Han S, Perry JS, Cartagena CM, Matsuura E, Maric D, Waldmann TA, Bielekova B. A role for interleukin-2 trans-presentation in dendritic cell-mediated T cell activation in humans, as revealed by daclizumab therapy. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/21532597) *Nat Med*. 2011 May;17(5):604-9.

Visit PubMed for a complete publication listing. ☐ (link is external) (https://www.ncbi.nlm.nih.gov/pubmed/?term=bielekova+b)

Clinical Research Protocols

Comprehensive Multimodal Analysis of Neuroimmunological Diseases of the CNS ☐ (link is external) (https://clinicalstudies.info.nih.gov/ProtocolDetails.aspx?A_09-I-0032.html%20@Internal@09-i-0032)

Targeting Residual Activity by Precision, Biomarker-Guided Combination Therapies of Multiple Sclerosis (TRAP-MS) ☐ (link is external)(https://clinicalstudies.info.nih.gov/ProtocolDetails.aspx?A_17-I-0083.html%20@Internal@17-i-0083)

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