NAME: Diaz-Mitoma, Francisco
POSITION TITLE: Chief Medical Officer, Future Dynamic Medicine, Inc.

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date (MM/YYYY)	FIELD OF STUDY
University of Guadalajara, Mexico	M.D.	07/1979	Medicine
University of Alberta, Canada	Ph.D.	09/1990	Medical Sciences (Virology)
University of Manitoba, Canada		07/1984	Fellowship in Infectious Diseases
Royal College of Physicians and Surgeons of Canada	Fellow	01/1990	Medical Microbiology

A. Personal Statement

I am a physician-scientist with over 25 years of experience in clinical research, viral immunology, vaccine development, cancer research, infectious diseases, molecular diagnostics, and translational medicine. My career has been dedicated to understanding viral pathogenesis and immune responses, particularly to herpesviruses like Epstein-Barr Virus (EBV) and Cytomegalovirus (CMV), and translating this knowledge into impactful vaccines and therapies. I have extensive expertise in designing and overseeing clinical trials (Phase 1 through 3), characterizing neutralizing antibody and T-cell responses, and leading the development programs for multiple licensed vaccines.

As Chief Medical Officer at VBI Vaccines (2015-2024), I directed the clinical development of novel vaccine candidates, including leading the teams that achieved licensure and commercial launch of PreHevbrio, the first 3-antigen Hepatitis B vaccine. My background also includes founding and leading research institutes like AMRIC in Ontario (now Health Sciences North Research Institute) and the Vaccine and Infectious Disease Centre at CHEO (Children's Hospital in Ottawa), and holding academic professorships. I have a strong publication record with over 150 peer-reviewed articles and have been recognized for contributions to science and global health.

I am particularly excited about the potential of the proposed project targeting the link between EBV and autoimmune disorders. This project directly aligns with my longstanding interest and expertise in herpesvirus immunology, vaccine design, and translational medicine. The novel dual-action therapeutic vaccine strategy, combining engineered EBV antigens with targeted tolerogenic delivery via lipid nanoparticles, represents a highly innovative and promising approach to address the root cause of EBV-triggered autoimmunity, a significant unmet medical need. My experience in clinical trial design, assay development for viral immunology, and

navigating regulatory pathways positions me well to contribute significantly to moving this precision immunotherapy towards clinical application. The potential to fundamentally alter disease trajectories for conditions like multiple sclerosis, rheumatoid arthritis, and lupus by restoring immune tolerance rather than relying on broad immunosuppression is profoundly motivating. I am eager to apply my expertise to optimize the vaccine formulations and advance this potentially transformative therapeutic strategy for patients.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

- 2024 – Present Chief Medical Officer, Future Dynamic Medicine, Inc., Ottawa, ON, Canada
- 2015 – 2024 Chief Medical Officer, VBI Vaccines, Inc.
- 2011 – 2018 Professor of Medical Sciences, Northern Ontario School of Medicine
- 2011 – 2015 Scientific Director and CEO, Advanced Medical Research Institute of Canada (AMRIC) / Health Sciences North Research Institute, Sudbury, ON, Canada
- 2011 – 2015 Vice President of Research, Health Sciences North
- 1995 – 2009 Medical Director & CEO, Herridge Health Ltd.
- 1990 – 2010 Professor of Pediatrics, Pathology, Laboratory Medicine, and Microbiology, University of Ottawa School of Medicine
- 1990 – 2008 Chief, Regional Virology Laboratory, University of Ottawa and Children's Hospital of Eastern Ontario (CHEO)
- 1990 – 2008 Chief, Department of Laboratory Medicine, University of Ottawa and Children's Hospital of Eastern Ontario (CHEO)
- (Date Unknown) Founder and Director, Vaccine and Infectious Disease Centre, Children's Hospital of Eastern Ontario (CHEO)
- (Date Unknown) Co-founder and former CEO, Variation Biotechnologies (now VBI Vaccines)
- (Date Unknown) Editorial Advisory Board Member for multiple scientific journals
- (Date Unknown) Board Member, Vaccine Infectious Disease Organization

Honors

- (Date Unknown) Ohtli Award
- (Date Unknown) "10 Most Influential Hispanics in Canada"
- (Date Unknown) American Society for Microbiology Young Investigator Award
- Fellow, Royal College of Physicians and Surgeons of Canada (FRCPC)

C. Contributions to Science

1. **Hepatitis B Vaccine Development and Immunology:** My research has significantly contributed to the development and understanding of hepatitis B vaccines, particularly focusing on multi-antigen approaches. This includes leading clinical trials for the 3-antigen vaccine (PreHevbrio/Sci-B-Vac™), demonstrating its superior immunogenicity,

safety profile, and long-term persistence of protective antibodies compared to single-antigen vaccines, especially in older adults and specific patient populations. We elucidated the immunological mechanisms, showing that the 3-antigen vaccine induces T-cell responses to PreS1 and PreS2 antigens, which correlate with higher and more durable anti-HBs antibody titers. Furthermore, cost-effectiveness analyses have highlighted the economic benefits of the 3-antigen vaccine in various countries.

- Berthoud TK, Ahmed T, Nadia W, Petrov I, Yang L, Colledge D, Plaksin D, Gillard P, **Diaz-Mitoma F**. A three antigen hepatitis B vaccine induces T cells to Pres1 and Pres2 which correlate with anti HBs antibody titers: An investigation into the immunological mechanisms. *Vaccine*. 2025;43:126513.
- Vesikari T, Langley JM, Popovic V, **Diaz-Mitoma F**. PreHevbrio: The first approved 3-antigen hepatitis B vaccine. *Expert Rev Vaccines*. 2023;22(1):1041-1054.
- **Diaz-Mitoma F**, Vesikari T, Berthoud T, Plaksin D, Anderson D, Popovic V. T-cell responses to PreS1 and PreS2 are correlated to anti-HBs antibody titres, which are higher and persist longer in volunteers vaccinated with 3-antigen than with 1-antigen HBV vaccine. *J Hepatol*. 2023;78:S1119.
- Vesikari T, Langley JM, Spaans JN, Petrov I, Popovic V, **Diaz-Mitoma F**. The persistence of seroprotective levels of antibodies after vaccination with PreHevbrio, a 3-antigen hepatitis B vaccine. *Vaccine*. 2023;41(24):3584-3588.
- Talbird SE, Anderson SA, Nossov M, Beattie N, Rak AT, **Diaz-Mitoma F**. Cost-effectiveness of a 3-antigen versus single-antigen vaccine for the prevention of hepatitis B in adults in the United States. *Vaccine*. 2023;41(23):3506-3517.
- Vesikari T, Forstén A, Popovic V, Spaans J, **Diaz-Mitoma F**. Long term persistence of anti-HBs antibodies after vaccination with a 3-antigen HBV vaccine compared to a single-antigen HBV vaccine. *J Hepatol*. 2022;77:S100-S101.
- **Diaz-Mitoma F**, Vesikari T, Langley J, Leroux-Roels I, Leroux-Roels G, et al. Cell-mediated and humoral immune responses after vaccination with a 3-antigen HBV vaccine containing Pre-S1, Pre-S2, and S antigens, compared to a single-antigen HBV vaccine. *Hepatology*. 2021;74:430A-430A.
- Vesikari T, Finn A, Van Damme P, Leroux-Roels I, Leroux-Roels G, **Diaz-Mitoma F**, et al. Immunogenicity and safety of a 3-antigen hepatitis B vaccine vs a single-antigen hepatitis B vaccine: a phase 3 randomized clinical trial. *JAMA Netw Open*. 2021;4(10):e2128652.
- Esaulenko EV, Yakovlev AA, Volkov GA, Sukhoruk AA, Surkov KG, Popovic V, **Diaz-Mitoma F**, et al. Efficacy and safety of a 3-antigen (pre-S1/pre-S2/S) hepatitis B vaccine: results of a phase 3 randomized clinical trial in the Russian Federation. *Clin Infect Dis*. 2021;73(9):e3333-e3339.

2. **CMV Vaccine Immunotherapy for Glioblastoma (GBM):** I have played a key role in the clinical development of VBI-1901, a cancer vaccine immunotherapeutic candidate

targeting Cytomegalovirus (CMV) antigens for recurrent GBM. This involved directing Phase 1/2a and Phase 2b clinical trials investigating the vaccine's safety, immunogenicity, tumor responses, and overall survival. Our research included comprehensive biomarker analyses to identify correlates of response, such as T-cell mediated collagen remodeling and specific immune signatures in responders versus non-responders, aiming to optimize patient selection and treatment strategies for this challenging malignancy.

- Merrell R, Wen P, Forst D, Schulte J, Odia Y, Bota D, Nagpal S, Bonm A, Lee E, Berthoud T, Roy E, Sore C, Reardon D, **Diaz-Mitoma F**. TUMOR RESPONSES IN A RANDOMIZED PHASE IIB TRIAL OF A CMV VACCINE IMMUNOTHERAPEUTIC CANDIDATE (VBI-1901) IN RECURRENT GLIOBLASTOMAS. *Neuro-Oncology*. 2024;26(Supplement_1):i10-i10. TPS2100.
- Merrell RT, Wen PY, Forst DA, Schulte J, Odia Y, Bota DA, **Diaz-Mitoma F**, et al. Randomized phase IIb trial of a CMV vaccine immunotherapeutic candidate (VBI-1901) in recurrent glioblastomas. *J Clin Oncol*. 2024;42(16_suppl):TPS2100.
- Iwamoto F, Nissen N, Reardon D, Forst D, Lee E, Berthoud T, Soare C, Roy E, **Diaz-Mitoma F**, Wen P. CTIM-27. PERIPHERAL BIOMARKER ANALYSIS OF T CELL-MEDIATED COLLAGEN REMODELING CORRELATES WITH TUMOR RESPONSES IN A PHASE IIA TRIAL OF VACCINE IMMUNOTHERAPEUTIC CANDIDATE (VBI-1901). *Neuro-Oncology*. 2023;25(Suppl 5):v68.
- Wen PY, Reardon DA, Forst D, Lee E, Daoud T, Berthoud T, Soare C, Roy E, **Diaz-Mitoma F**. CTIM-14. COMPREHENSIVE BIOMARKER ANALYSIS OF RESPONDERS AND NON-RESPONDERS IN A PHASE IIA TRIAL OF A CMV VACCINE IMMUNOTHERAPEUTIC CANDIDATE (VBI-1901). *Neuro-Oncology*. 2022;24(Suppl 7):vii62.
- Wen PY, Reardon DA, Forst DA, Lee EQ, Haas B, Daoud T, Berthoud T, Roy E, Soare C, **Diaz-Mitoma F**. Evaluation of tumor responses and overall survival in patients with recurrent glioblastoma (GBM) from a phase IIa trial of a CMV vaccine immunotherapeutic candidate (VBI-1901). *J Clin Oncol*. 2022;40(16_suppl):2014.

3. **Virology, Diagnostics, and Vaccine Platforms:** My career has included foundational work in virology diagnostics and the development of vaccine platforms. I have specific expertise in herpesviruses, including CMV and Epstein-Barr virus (EBV), focusing on viral pathogenesis, immune responses, and the development of diagnostic tools and vaccine candidates. This includes research on enveloped virus-like particles (eVLPs) as a versatile platform for vaccine development, applicable to various infectious diseases and potentially cancer immunotherapy.

   - **Diaz-Mitoma F**. Enveloped virus-like particles as a platform for vaccine development. *Int J Noncommunicable Dis*. 2021;6(Suppl 1):S89-S94.

    - Lewicky JD, Martel AL, Fraleigh NL, Picard E, Mousavifar L, Nakamura A, Roy E, **Diaz-Mitoma F**, et al. Exploiting the DNA damaging activity of liposomal low dose cytarabine for cancer immunotherapy. *Pharmaceutics*. 2022;14(12):2710.
4. **Leadership in Research Infrastructure and Translational Medicine:** Beyond specific scientific contributions, I have demonstrated leadership in building research capacity and fostering translational medicine. As the founder and CEO of the Advanced Medical Research Institute of Canada (AMRIC), I led initiatives to establish a major research facility, develop advanced diagnostic tools, and integrate research into the health system in Northern Ontario. This involved managing multidisciplinary teams, securing funding, and driving innovation from the bench to clinical application. My experience spans academic leadership, directorship of clinical laboratories, and executive roles in biotechnology.

D. Additional Information: Research Support and/or Scholastic Performance

- *Clinical development program for PreHevbrio (3-Antigen Hepatitis B Vaccine) during tenure as CMO at VBI Vaccines (2015-2024).*
- *Clinical development program for VBI-1901 (CMV Vaccine Immunotherapeutic for GBM) during tenure as CMO at VBI Vaccines (2015-2024).*
- *Leadership of clinical and translational research initiatives at AMRIC/HSNRI (2011-2015).*
- *Direction of virology research and diagnostics at University of Ottawa/CHEO (1990-2008).)*