BIOGRAPHICAL SKETCH

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NAME: Matoba, Nobuyuki

eRA COMMONS USER NAME (credential, e.g., agency login): nmatoba

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Kyoto University, Kyoto, Japan	B.S.	3/1996	Food Science and Technology
Kyoto University, Kyoto, Japan	M.S.	3/1998	Applied Life Science
Kyoto University, Kyoto, Japan	Ph.D.	3/2001	Applied Life Science
Arizona State University, AZ	Postdoctoral	3/2004	Plant Biotechnology and Vaccinology

A. Personal Statement

I have expertise in biotechnology, protein engineering and biopharmaceutical science. My research over the past 20 years has focused on the development of mucosal vaccines and biotherapeutics against HIV and other viral pathogens, inflammatory bowel disease and cancer. We have substantial experience with transient overexpression systems in *Nicotiana benthamiana* plants, which enable efficient production and characterization of novel recombinant proteins (*1*). We recently engineered two unique biopharmaceutical candidates, exhibiting anti-viral/tumor activity (Avaren-Fc "LECTIBODY"; *2, 3*) and mucosal healing activity (a KDEL-tagged cholera toxin B subunit variant; *4, 5*). The latter project has reached a milestone where we have submitted a pre-IND package to U.S. FDA for a first-in-human clinical trial. In addition to these projects, I am leading the Pharmacokinetics/Pharmacodynamics Core of a NIH U19-funded Phase I clinical trial project for a HIV topical microbicide based on the antiviral protein griffithsin, overseeing Quality Control activities of the drug substance/product as well as pharmacokinetics and immunogenicity assay development. Building on this experience, I have served as a reviewer on a NIH Special Emphasis Review Panel for a UM1 sustained-release anti-HIV drug development/Phase I clinical trial grant program. In summary, I have substantial experience and unique expertise in biopharmaceutical discovery and development.

1. **Matoba N***, Davis KR, Palmer KE. (2011) Recombinant Protein Expression in Nicotiana. *Methods Mol Biol*. 701:199-219.
2. Hamorsky KT, Kouokam JC, Dent WD, Grooms TN, Husk AS, Hume SD, Rogers KA, Villinger F, Morris MK, Hanson CV, **Matoba N***. (2019) Engineering of a lectibody targeting high-mannose-type glycans of HIV envelope. *Mol Ther* 27(11):2038-2052. PMCID: PMC6839005
3. Dent M, Hamorsky KT, Vausselin T, Dubuisson J, Miyata Y, Morikawa Y, **Matoba N***. (2020) Safety and Efficacy of Avaren-Fc Lectibody Targeting HCV High-Mannose Glycans in a Human Liver Chimeric Mouse Model. (2020) *Cell Mol Gastroenterol Hepatol* in press.
4. Baldauf KJ, Royal JM, Kouokam JC, Haribabu B, Jala VR, Yaddanapudi K, Hamorsky KT, Dryden GW, **Matoba N***. (2017) Oral administration of a recombinant cholera toxin B subunit promotes mucosal healing in the colon. *Mucosal Immunol* 10: 887-900
5. Royal JM, Oh YJ, Grey MJ, Lencer WI, Ronquillo N, Galandiuk S, **Matoba N***. (2019) A modified cholera toxin B subunit containing an ER retention motif enhances colon epithelial repair via an unfolded protein response. *FASEB J* 33(12):13527-13545.

B. Positions and Honors

Positions and Employment

4/2004 – 12/2005	Faculty Research Associate, School of Life Sciences, Arizona State University
1/2006 – 9/2008	Research Assistant Professor, Biodesign Institute, Arizona State University
10/2008 – 12/2013	Assistant Professor (tenure track) of Pharmacology & Toxicology, University of Louisville School of Medicine, Louisville, KY
1/2014 – 6/2019	Associate Professor (tenured) of Pharmacology & Toxicology, University of Louisville School of Medicine
7/2019 – present	Professor (tenured) of Pharmacology & Toxicology, University of Louisville School of Medicine
7/2019 – present	Founding Member and Chief Scientific Officer, Grow Biomedicine LLC, Louisville, KY

Professional Memberships

2008 – present	Member, Society for Mucosal Immunology
2013 – present	Member, American Society for Microbiology
2018 – present	Member, American Gastroenterological Association

Grant review panel

2011	Grant reviewer, National Research Foundation, the Republic of South Africa
2013	Grant reviewer, the Nazarbayev University Research Council in Astana, Kazakhstan
2015	NIH/NIAID Special Emphasis Review Panel (ZAI1-JBS-A-M1), Sustained Release for Antiretroviral Treatment or Prevention (SRATP) of HIV Infection (UM1)
2016	NIH/NIAID Special Emphasis Review Panel (ZRG1 AARR-M54), Non-vaccine Biomedical Prevention (nBP) of HIV acquisition/transmission (R01)
2017	Grant reviewer, Natural Sciences And Engineering Research Council (NSERC) Collaborative Research and Development (CRD) Grant Program, Canada

Journal Editorial Board

2015 – present	Editorial Board Member, *Scientific Reports*
2017 – present	Associate Editor, *Frontiers in Plant Science*

Honors and Awards

2000 – 2002	Japan Society for the Promotion of Science (JSPS) Research Fellowship for Young Scientist
2004 – 2006	JSPS Postdoctoral Fellowship for Research Abroad
2005	Keystone Symposia HIV Vaccines Travel Award
2005	Society for Mucosal Immunology Young Investigator Award
2008	Keystone Symposia Scholarship for Fellows and New Investigators Workshop on Grantsmanship and Career Research Opportunities in HIV/AIDS Research
2009	3rd place, Roger H. Herzig Junior Faculty Research Prize, James Graham Brown Cancer Center
2010	International Microbicide Conference Scholarship
2014	Scientist of the Year, University of Louisville Brown Cancer Center

Patents

- Patent Number: US 7,438,914 (granted on Oct 21, 2008)
  Composition and method for enhancing immune response
- Patent Number: US 8,802,822 B2 (granted on Aug 12, 2014)
  Polypeptides having antiviral activity and methods for use thereof
- Patent Number: US 9,133,252 B2 (granted on Sep 15, 2015)
  Polypeptides having antiviral activity and methods for use thereof
- Patent Number: US 10,066,238 (granted on Sep 4, 2018)
  Methods of producing antibodies
- Patent Number: US 10,160,789 B2 (granted on Dec 25, 2018)
  Polypeptides having immunoactivating activity and methods of producing the same
- Application No. PCT/US2016/040041 (*Notice of allowance received on 4/3/2020)
  Compositions and methods for treating cancer and promoting wound healing
- Application No. PCT/US2018/017617

Actinohivin variant polypeptides and related methods

Entrepreneurial and Other Activity Related to Profession and Expertise

4/2019 – present	Co-founder and Chief Scientific Officer, Grow Biomedicine, LLC (Kentucky, USA)
4/2019 – present	Expert witness in a civil litigation (iBio, Inc. v. Fraunhofer USA, Inc., C.A. No. 10256-VCMR)

C. Contributions to Science

1. My early publications as a graduate student at Kyoto University in Japan addressed the identification and characterization of health-promoting factors in food proteins, particularly bioactive peptides that have the capacity to modulate physiological activities in humans (**a**). My PhD study has focused on a hexapeptide derived from the egg protein ovalbumin, RADHPF. In a spontaneously hypertensive rat model, oral administration of the peptide was shown to exhibit vasorelaxation activity via the induction of nitric oxide in the endothelial cells, leading to the mitigation of hypertension (**b**). Subsequently, we engineered a novel anti-hypertensive peptide based on a structure-activity relationship analysis of RADHPF, and the resultant peptide was incorporated into the soybean protein β-conglycinin α' subunit through genetic engineering. The modified soybean protein was shown to lower blood pressure in hypertensive rats, suggesting that the protein could be used as a functional food component to mitigate hypertension (**c, d**).

    a. Yoshikawa M, Fujita H, **Matoba N**, Takenaka Y, Yamamoto T, Yamauchi R, Tsuruki T, Takahata K. (2000) Bioactive peptides derived from food proteins preventing lifestyle-related diseases. *BioFactors* 12:143-146.
    b. **Matoba N**, Usui H, Fujita H, Yoshikawa M. (1999) A novel anti-hypertensive peptide derived from ovalbumin induces nitric oxide-mediated vasorelaxation in an isolated SHR mesenteric artery. *FEBS Lett*. 452:181-184.
    c. **Matoba N**, Doyama N, Yamada Y, Maruyama N, Utsumi S, Yoshikawa M. (2001). Design and production of genetically modified soybean protein with anti-hypertensive activity by incorporating potent analogue of ovokinin (2-7). *FEBS Lett* 497:50-54.
    d. **Matoba N**, Yamada Y, Yoshikawa M. (2003) Design of a genetically modified soybean protein preventing hypertension based on an anti-hypertensive peptide derived from ovalbumin. *Curr Med Chem-Cardiovasc & Hematol Agents* 1:197-202.

2. After completion of my PhD research, I have worked on plant-made protein pharmaceuticals research as a postdoc scientist and later as a research faculty member at Arizona State University Biodesign Instutute. My main project was focused on creating transgenic plants expressing a mucosal vaccine against HIV/AIDS with the ultimate goal of developing an inexpensive plant-made oral HIV vaccine. We designed an immunogen based on a peptide spanning the conserved membrane proximal region (MPR) of the envelope glycoprotein gp41, which was genetically fused to a non-toxic mucosal immuno-stimulatory protein, cholera toxin B subunit (CTB). We demonstrated that the CTB-MPR fusion protein can elicit HIV transmission-blocking antibodies and that the protein can be stably expressed in transgenic tobacco plants (**a, b**). In 2007 I have acquired my first NIH grant for the development of an HIV virus-like particle (VLP) vaccine in plants. We have successfully generated a chimeric VLP immunogen consisting of HIV Gag and MPR in plants (**c, d**).

    a. **Matoba N**, Magérus A, Geyer BC, Zhang Y, Muralidharan M, Alfsen A, Arntzen CJ, Bomsel M, Mor TS. (2004) A mucosally targeted subunit vaccine candidate eliciting HIV-1 transcytosis-blocking Abs. *Proc Natl Acad Sci USA* 101:13584-13589. PMCID: PMC518798
    b. **Matoba N**, Kajiura H, Cherni I, Doran JD, Bomsel M, Fujiyama K, Mor TS. (2009) Biochemical and immunological characterization of the plant-derived candidate human immunodeficiency virus type 1 mucosal vaccine CTB-MPR649-684. *Plant Biotechnol J* 7(2):129-145.
    c. Kessans SA, Linhart MD, **Matoba N***, Mor TS*. (2013) Biological and biochemical characterization of HIV-1 Gag/dgp41 virus-like particles expressed in Nicotiana benthamiana. *Plant Biotechnol J* 11(6)681-90. *Co-corresponding authors. PMCID: PMC3688661 *Co-senior/corresponding authors
    d. Kessans SA, Linhart MD, Meador LR, Kilbourne J, Hogue BG, Fromme P, **Matoba N**, Mor TS. (2016) Immunological Characterization of Plant-Based HIV-1 Gag/Dgp41 Virus-Like Particles. *PLoS ONE* 11(3):e0151842. PMCID: PMC4795674

3. In October 2008 I have joined the faculty of Department of Pharmacology and Toxicology at the University of Louisville School of Medicine. My lab is specialized in plant-made protein pharmaceuticals research, with the mission of developing vaccines, immunotherapeutics, and antivirals based on protein engineering and plant biotechnology. Currently, we have two main projects:

   (1) High-mannose glycan-binding lectins and lectibodies. Asparagine-linked high-mannose-type glycans constitute unique biomarkers on the surfaces of enveloped viruses (e.g., HIV, HCV, SARS-CoV, influenza, etc) and cancer cells. The actinomycete-derived lectin actinohivin exhibits anti-HIV activity via binding to viral high-mannose glycan clusters. We have characterized the anti-HIV activity, safety and plant-producibility of actinohivin (**a**). Meanwhile, we have successfully developed a novel method to produce human IgG monoclonal antibodies in plants, which enables rapid and scalable manufacturing of therapeutic antibodies. Combining the actinohivin findings and the antibody production technology, we have developed a novel lectin-antibody fusion protein, Avaren-Fc "lectibody" (**b**). The lectibody was shown to effectively recognize high-mannose glycans on viruses and cancer cells, exhibit potent antiviral activity against HIV and hepatitis C virus, and facilitate NK cell's cancer killing activity. Collectively, the lectibody could be developed as a new antiviral and/or a cancer immunotherapeutic/diagnostic agent.

   (2) Enterotoxin-derived immunomodulatory proteins. Bacterial enterotoxins are known to elicit strong immunostimulatory effects. These proteins may be exploited to enhance vaccine efficacy or to control deregulated immune activities of various autoimmune disorders. We have recently developed a robust and rapid plant-based recombinant production platform for a variant of cholera toxin B subunit, CTB^{SEKDEL} (**c**). Since recombinant CTB is currently used in the internationally licensed oral cholera vaccine Dukoral®, CTB^{SEKDEL} could provide an alternative cholera vaccine antigen to aid in mass vaccination against cholera outbreaks. Additionally, we have recently shown that CTB^{SEKDEL} facilitates mucosal healing in colitis models (**d**), suggesting that CTB^{SEKDEL} could be developed as a novel oral biotherapeutic for IBD.

   a. **Matoba N***, Husk AS, Barnett BW, Pickel MM, Arntzen CJ, Takahashi A, Tanno K, Omura S, Montefiori DC, Mooney JP, Cao H, Hanson CV, Tanaka H. (2010) HIV-1 Neutralization Profile and Plant-based Recombinant Expression of Actinohivin, an Env Glycan-specific Lectin Devoid of T-cell Mitogenic Activity. *PLoS ONE* 5(6): e11143. PMCID: PMC2886112
   b. Hamorsky KT, Kouokam JC, Dent MW, Grooms TN, Husk AS, Hume SD, Rogers KA, Villinger F, Morris MK, Hanson CV, **Matoba N***. (2019) Engineering of a lectibody targeting high-mannose-type glycans of HIV envelope. *Mol Ther* 27(11):2038-2052. PMCID: PMC6839005
   c. Hamorsky KT, Kouokam JC, McMullen J, Nelson B, Bennett L, Husk A, Kajiura H, Fujiyama K, **Matoba N***. (2015) N-Glycosylation of cholera toxin B subunit in Nicotiana benthamiana: impacts on host stress response, production yield and vaccine potential. *Sci Rep* 5: 8003. PMCID: PMC4303877
   d. Royal JM, Oh YJ, Grey MJ, Lencer WI, Ronquillo N, Galandiuk S, **Matoba N***. (2019) A modified cholera toxin B subunit containing an ER retention motif enhances colon epithelial repair via an unfolded protein response. *FASEB J* 33(12):13527-13545.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/nobuyuki.matoba.1/bibliography/43900491/public/?sortby=pubDate&sdirection=descending

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

Ongoing

U19AI113182 Palmer (PD)/Matoba (Core C PI) 07/01/14 – 06/30/20 (currently NCE)
NIH/NIAID
"Griffithsin-based Rectal Microbicides for PREvention of Viral ENTry (PREVENT)"
This program project's goal is to determine the feasibility of the antiviral protein griffithisin as a microbicide gel product against rectal transmission of HIV in non-human primate studies and in a first-in-human clinical trial.
Role: PI of Pharmacokinetics and Pharmacodynamics Core (Core C)

1R21CA216447-01A1 Matoba (PI) 02/08/18 – 1/31/2020 (currently NCE)
NIH/NCI
"Investigation of a lectibody targeting tumor-associated oligomannose glycans"

The goal of this project is to investigate the anti-cancer therapeutic and diagnostic potentials of Avaren-Fc lectibody.
Role: PI

1 R01 DK123712-01A1 Matoba (PI) 07/01/20 – 03/31/24
NIH/NIDDK
"Preclinical validation of oral therapeutic lead proteins targeting epithelial GM1 ganglioside for ulcerative colitis therapy"
The goal is to optimize and validate the draggability of recombinant protein CTB^{SEKDEL} using in vitro assays, murine colitis models and human colonic explants for the development of a novel oral biotherapeutic for the treatment of ulcerative colitis.
Role: PI

Completed (past 3 years)

U01HL127518-01 Bates/Miller/Krentsel (co-PIs) 02/01/2016 – 3/20/2018
NIH/NIHLB $200,000 (subproject direct cost)
Title: The EXCITE Program: Expediting Commercialization, Innovation, Translation and Entrepreneurship
Subproject title: Oral solid dosage formulation of cholera toxin B subunit
This project develops a dry-formulated enteric-coated cholera toxin B subunit for oral delivery.
Role: Subproject co-PI (with Hamorsky)

U01HL127518-01 Bates/Miller/Krentsel (co-PIs) 03/01/2017 – 6/30/2018
NIH/NIHLB $150,000 (subproject direct cost)
Title: The EXCITE Program: Expediting Commercialization, Innovation, Translation and Entrepreneurship
Subproject title: Investigation of a lectibody targeting tumor-associated oligomannose glycans
This project investigates anti-HCV activity of Avaren-Fc lectibody in a chimeric mouse model for transplant liver protection.
Role: Subproject PI (with Hamorsky)

U01HL127518-01 Bates/Miller/Krentsel (co-PIs) 08/01/2017 – 7/31/2018
NIH/NIHLB $100,000 (subproject direct cost)
Title: The EXCITE Program: Expediting Commercialization, Innovation, Translation and Entrepreneurship
Subproject title: Topical application of CTBp for oral mucositis treatment
This project investigates the efficacy of a cholera toxin B subunit variant upon topical application in animal models of mucositis.
Role: Subproject PI (with Hamorsky)

2014PG-MED001 Matoba (PI) 12/01/19 – 7/31/20
Leona M. and Harry B. Helmsley Charitable Trust
Project title: Advancing the discovery and development of plant-made pharmaceuticals
The objectives are to develop preclinical data, to refine a regulation-compliant manufacturing process, and to prepare a pre-IND Briefing Document towards a first-in-human clinical trial of EPICERTIN enema product.
Role: PI