BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Alison A. McCormick	Professor
eRA COMMONS USER NAME	
AMCCORPI	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Iowa State University at Ames	B.S.	1979-1984	Biological Psychology
University of California at San Diego	Ph.D.	1985-1990	Pharmacology
Stanford University School of Medicine	Post doc	1990-1995	Developmental Biology
Stanford University School of Medicine	Visiting Sch.	1996-2001	Vaccine Development

A. Personal Statement.

I have been working in vaccine development for more than two decades, using a novel viral carrier to promote innate and adaptive immunity. I use Tobacco Mosaic Virus (TMV) as an adjuvant to subunit and peptide vaccines to promote optimized antigen delivery and stimulate effective neutralizing immune responses. By chemically conjugating subunit proteins or peptides to the TMV surface, I can create vaccines that induce robust and balanced cellular and humoral immunity, regardless of the subunit protein identity or initial immune potency. I am currently engaged in a number of collaborations which focus on preparation and testing of vaccines in pathogen challenge settings. I have an extensive collaboration with Dr. Paul Arnaboldi at NY Medical College, who is an expert in *Yersinia pestis* (Yp) pathogenicity, immunity, and pathogen challenge, and we have a long-standing track record of success in vaccine development. More recently, we are working together in collaboration with Dr. Adriana Kajon at the Lovelace Biomedical to develop an Adenovirus specific TMV-peptide vaccine. We have recently shown that TMV-peptide conjugates can stimulate neutralizing antibodies to Adenovirus infection, and expect further work to refine and improve vaccine efficacy. TMV-Ag conjugate vaccines are safe and effective as multi-antigen compositions, which will allow for improved vaccine breadth and potency, to respond to an unmet need for vaccines against currently circulating infectious diseases.

B. Positions and Honors.

2023 to present	**Adjunct Professor**, Chemical Engineering, University of California, Davis
2023 to present	**Adjunct Professor**, Touro University, College of Pharmacy
2007 to 2023	**Professor**, Touro University, College of Pharmacy
2010-23	**USP delegate**
2006-12	**Associate Professor**; Touro University, College of Pharmacy
2004-06	**Principal Scientist**; Preclinical Development, LSBC
1996-04	**Senior Scientist**; Large Scale Biology, Inc. (LSBC)
1996-01	**Visiting Scholar**; Stanford University School of Medicine
1995-96	**Scientist**; Tularik, Inc.
1994-95	**Howard Hughes Research Fellow**; Stanford University School of Medicine
1993-94	**Katharine McCormick Scholar**; Stanford University School of Medicine
1990-93	**Jane Coffin Childs Postdoctoral Fellow**; Stanford University School of Medicine

C. Contributions to Science (in chronological order).

1. Single chain antibody idiotype vaccine production in plants, and use in a phase I clinical trial to treat Non-Hodgkin's lymphoma patients

Vaccination with human hybridoma produced IgG was shown to successfully improve clinical outcome in non-Hodgkin's lymphoma patients, and was one of the first cancer vaccines to show promise in the clinic. Our goal was to speed time to production and replace full IgG molecules with just the tumor-specific Fv region as a single chain antibody. Preliminary data suggested that bacterial produced scFv proteins were not conformationally relevant to the tumor Ig, so the second goal was to develop a eukaryotic expression

system that would allow for proper scFv folding. To accomplish this, we optimized a plant expression system based on Tobacco Mosaic Virus (1). One major contribution of our work was a demonstration that proper Fv folding required a variable linker length and composition (2), and that 95% of scFv could be made in plants at high yield using this strategy. A second major contribution was the bench to bedside production and testing of 16 patient-specific scFv vaccines in a Phase I clinical trial. Our trial was a landmark trial, as this was the first FDA-approved parenteral administration of a plant-made biologic. We confirmed both safety and efficacy in vaccinated patients (3). This work has also contributed to the on-going use of plant-produced NHL therapy (4).

a. **McCormick AA**, Kumagai MH, Hanley K, Turpen TH, Hakim I, et al. Rapid production of specific vaccines for lymphoma by expression of the tumor-derived single-chain Fv epitopes in tobacco plants. Proceedings of the National Academy of Sciences of the United States of America. 1999; 96(2):703-8. PMID: 9892697,

b. **McCormick AA**, Reinl SJ, Cameron TI, Vojdani F, Fronefield M, et al. Individualized human scFv vaccines produced in plants: humoral anti-idiotype responses in vaccinated mice confirm relevance to the tumor Ig. Journal of immunological methods. 2003; 278(1-2):95-104. PMID: 12957399

c. **McCormick AA**, Reddy S, Reinl SJ, Cameron TI, Czerwinkski DK, et al. Plant-produced idiotype vaccines for the treatment of non-Hodgkin's lymphoma: safety and immunogenicity in a phase I clinical study. Proceedings of the National Academy of Sciences of the United States of America. 2008;105(29):10131-6. PMID: 18645180,

d. Bendandi M, Marillonnet S, Kandzia R, Thieme F, Nickstadt A, et al. Rapid, high-yield production in plants of individualized idiotype vaccines for non-Hodgkin's lymphoma. Annals of oncology (ESMO). 2010; 21(12):2420-7. PMID: 20494963

2. TMV as an antigen carrier for peptides are effective anti-cancer agents

Cancer vaccines are most effective when cellular immunity is activated. We used a strategy to link cancer-related peptides to the surface of TMV, to provide both antigen uptake and activation. We have demonstrated that TMV interacts directly with murine antigen presenting cells, including dendritic cells, and up-regulates surface markers of activation (1) and significantly improve protection in a murine model of melanoma (2) and in a rabbit model of papillomavirus induced malignancy (3). TMV-peptide fusions are as effective as live replicating adenovirus infection in inducing activated T cells, without a corresponding anamnestic response (4).

a. **McCormick AA**, Corbo TA, Wykoff-Clary S, Palmer KE, Pogue GP. Chemical conjugate TMV-peptide bivalent fusion vaccines improve cellular immunity and tumor protection. Bioconjugate chemistry. 2006; 17(5):1330-8. PMID: 16984144

b. Palmer KE, Benko A, Doucette SA, Cameron TI, Foster T, Foster T, Hanley KM, **McCormick AA**, et al. Protection of rabbits against cutaneous papillomavirus infection using recombinant tobacco mosaic virus containing L2 capsid epitopes. Vaccine. 2006; 24(26):5516-25. PMID: 16725236

c. Kemnade JO, Seethammagari M, Collinson-Pautz M, Kaur H, Spencer DM, **McCormick AA**. Tobacco mosaic virus efficiently targets DC uptake, activation and antigen-specific T cell responses in vivo. Vaccine. 2014; 32(33):4228-33. PMID: 24923637

d. Soo Hoo, W, Higa K, **McCormick AA**. Vaccination against Epstein-Barr Latent Membrane Protein 1 Protects against an Epstein-Barr Virus-Associated B Cell Model of Lymphoma. MDPI Biology (Basel). 2023 12(7):983. PMID: 37508413

3. TMV as an antigen carrier for RNA-based vaccines

TMV coat protein exhibits one of the best characterized self-assembly processes, and depends entirely on the presence of an origin of assembly (OA) in the 3' end of the TMV genomic RNA. We took advantage of the sequence independence of the OA to confer coat protein self-assembly onto a non-TMV RNA, initially SFV. The goal was to make an RNA vaccine using a replicating but non-infectious virus, and provide that RNA in a package that would target antigen presenting cell uptake (1). We then explored the ability of the TMV OA to confer self assembly of an RNA backbone from Flock House virus (FHV), which is very small RNA genome, and much easier to genetically manipulate, with less apoptosis than SFV (2). We were then able to adapt this smaller RNA to an *in vivo* encapsidation system in plants, using a two component expression system, one to express TMV coat, and one to express the FHV-OA genomic RNA. The goal

was to produce fully capped RNA to improve translation efficiency, and overcome obstacles of *in vitro* RNA synthesis. Both goals were accomplished, and immunogenicity to the transgene was confirmed (3).

a. Smith ML, Corbo T, Bernales J, Lindbo JA, Pogue GP, Palmer KE, **McCormick AA**. Assembly of trans-encapsidated recombinant viral vectors engineered from Tobacco mosaic virusand Semliki Forest virus and their evaluation as immunogens. Virology. 2007;358(2):321-33. PMID: 17014881

b. Maharaj PD, Mallajosyula JK, Lee G, Thi P, Zhou Y, Kearney CM, **McCormick AA**. Nanoparticle encapsidation of Flock house virus by auto assembly of Tobacco mosaic virus coat protein. International journal of molecular sciences. 2014; 15(10):18540-56. PMID: 25318056

c. Zhou Y, Maharaj PD, Mallajosyula JK, **McCormick AA**, Kearney CM. In planta production of flock house virus transencapsidated RNA and its potential use as a vaccine. Molecular biotechnology. 2015; 57(4):325-36. PMID:25432792

4. TMV as an antigen carrier for whole protein vaccines

It is well established that proteins, though safe and well defined vaccine agents, typically elicit very weak immune responses, probably due to limited activation of innate danger signals. Our goal was to improve protein vaccination by improving innate immune uptake and activating characteristics, using TMV virus as a carrier to augment immunogenicity. We have shown in preliminary studies that TMV provides extensive surface area for antigen linkage, and physical association of proteins to TMV surface augments immunogenicity of a model antigen. We have further explored different linkage chemistries using an HA protein antigen relevant to Influenza A H1N1, and demonstrated significant improvements in survival from pathogen challenge after single low dose vaccinations (1). More recently, we have used TMV as a carrier for antigens from highly pathogenic *Francisella tularensis*, that isn't suitable for attenuation (2), and showed good protection from pathogen challenge by subcutaneous (2) or intranasal dosing (4). Protection against Yersinia pestis challenge was 100% after two doses of vaccination (3). Lastly, six different Tuberculosis antigens have been tested as TMV-Ag vaccines, with 100-1000 fold improvement in cellular and humoral immunity, with challenge studies in process (manuscript in preparation).

a. Mallajosyula JK, Hiatt E, Hume S, Johnson A, Jeevan T, Chikwamba R4, Pogue GP5, Bratcher B2, Haydon H, Webby RJ, **McCormick AA**. Single-dose monomeric HA subunit vaccine generates full protection from influenza challenge. Human vaccines & immunotherapeutics. 2014; 10(3):586-95. PMID:24378714

b. Arnaboldi PM, Sambir M, D'Arco C, Peters LA, Seegers JF, Mayer L, **McCormick AA**, Dattwyler RJ. Intranasal delivery of a protein subunit vaccine using a Tobacco Mosaic Virus platform protects against pneumonic plague. Vaccine. 2016 Nov 11;34(47):5768-76. PMID: 27745954

c. **McCormick, AA**., Shakeel, A., Yi, C., Kaur, H., Mansour, AM., and Bakshi, CS. Intranasal administration of a two-dose adjuvanted multi-antigen TMV-subunit conjugate vaccine fully protects mice against Francisella tularensis LVS challenge.PLOS One, 2018 Apr 23;13(4):e0194614. PMID: 29684046

d. **McCormick, AA**., Shakeel, A., Yi, C., Kaur, H., Mansour, AM., and Bakshi, CS. Intranasal administration of a two-dose adjuvanted multi-antigen TMV-subunit conjugate vaccine fully protects mice against Francisella tularensis LVS challenge. PLOS One, 2018 Apr 23;13(4):e0194614. PMID: 29684046

e. D'Arco C, **McCormick AA**, Arnaboldi PM. Single-dose intranasal subunit vaccine rapidly clears secondary sepsis in a high-dose pneumonic plague infection. Vaccine. 2021;39(9):1435-1444. PMID: 33531196

f. Royal JM, Simpson CA, **McCormick AA**, Phillips A, Hume S, Morton J, Shepherd J, Oh Y, Swope K, DeBeauchamp JL, Webby RJ, Cross RW, Borisevich V, Geisbert TW, Demarco JK, Bratcher B, Haydon H, Pogue GP. Development of a SARS-CoV-2 Vaccine Candidate Using Plant-Based Manufacturing and a Tobacco Mosaic Virus-like Nano-Particle. Vaccines (Basel). 2021 Nov 17;9(11):1347. PMID: 34835278

My full bibliography is available at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/alison.mccormick.1/bibliography/41138991/public/?sort=date&direction=ascending

D. Current Research Support

TUC/Lovelace foundation grant McCormick, Alison A., co-PI 08-2024 to 07-2025
"Development of a broadly protective adenovirus vaccine"
The major goals of this project will be to test TMV-peptide conjugate vaccines to focus host immunity on consensus amino acid sequences multiple clades of adenovirus, within key target regions of proteins that are involved in virus entry, virus replication, or virus pathogenicity. Testing will include virus neutralization of homologous and heterologous virus types of adenovirus, and protection from virus challenge in small animal models of infection.

R01 AI147109-01A1 McCormick, Alison A., co-PI 07-2020 to 06-2025
"Rapid Manufacturing of a Universal Flu Vaccine Using TMV-conjugated Centralized Antigens"
The major goals of the project will be to use a consensus HA strategy to produce a TMV-HA vaccine capable of stimulating broadly neutralizing antibodies, against homologous and non-homologous Influenza A virus strain. The goal will be to combine TMV-HA consensus vaccines with universal antigens, like M2e or NA, and test the efficacy of vaccine combinations for immunogenicity and protection from homologous and heterologous virus challenge.

D. Completed Research Support

NIH/NIAID McCormick, Alison A., Co-PI 1-2021 to 6-2024
1 R21 AI164233-01A1
" Novel Mucosal Vaccine for Pseudomonas aeruginosa Infection "
The major goals of the project will be to develop and optimize antigen formulations to vaccinate against virulent Pseudomonas lethal infection.

NIH/NIAID McCormick, Alison A., Co-PI 06-2016 to 05-2019
1 R21 AI122108-01A1
"Preclinical Development of a Multivalent Tularemia Vaccine"
The major goals of the project will be to develop and optimize antigen formulations to protect against virulent Francisella Tularensis lethal infection.

NIH/NIAID McCormick, Alison A., PI 1-2015 to 12-2017
1 R21 AI121749
"Virus-DNA-Virus hybrid vaccines for the prevention of Influenza"
The major goals of the project will be to develop TMV as a way to delivery DNA vaccines directly to antigen presenting cells. Vaccines will be used to protect mice from H5N1 and H7N9 influenza challenge, in collaboration with Dr. Richard Webby, St. Jude Children's Research Hospital.

Gates Grand Challenge McCormick, Alison A., PI 05-2012 to 10-2013
Synthetic Biology, OPP1059735
"Plant-produced synthetic RNA vaccines"
The major goals of the project will be to develop an *in vivo* transencapsidation system in plants, to create novel combinations of RNA and TMV coat protein for Malaria vaccine optimization *in vivo*.

NIH/NCI McCormick, Alison A., PI 10-2008 to 9-2011
R21CA141094-01
"Improved idiotype immunotherapy for lymphoma by RNA vaccine delivery"
The major goals of the project will be to develop an *in vivo* transencapsidation system in plants, to create novel combinations of RNA and TMV coat protein for lymphoma vaccine optimization *in vivo*.