BIOGRAPHICAL SKETCH

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NAME: McDonald, Karen A.

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Feb 27, 2018

POSITION TITLE: Professor, Chemical Engineering

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
Stanford University, Stanford, CA	B.S.	06/1979	Chemical Engineering
University of California, Berkeley, CA	M.S.	06/1980	Chemical Engineering
University of Maryland, College Park, MD	Ph.D.	12/1985	Chemical Engineering

A. Personal Statement

I have been applying synthetic biology tools in plants for the development of novel expression systems as well as applying bioprocess engineering technologies to produce recombinant proteins (including human therapeutic proteins, enzymes for cellulose degradation, and bioscavengers for use as medical countermeasure protection agents biothreats) using whole plants, harvested plant tissues or plant cells grown *in vitro* in bioreactors as hosts. As a biochemical engineer, I am interested in translational research and continually strive to develop processes that are scalable, cost effective, and meet quality specifications and regulatory requirements. I have extensive experience in production, scale-up, purification and characterization of heterologous proteins using transient expression in plants as well as transgenic plant cell suspension cultures in bioreactors, and performing techno-economic analyses. I am a member of the graduate program/groups in Chemical Engineering, Biomedical Engineering and Plant Biology as well as the Designated Emphasis in Biotechnology. I formerly served as the Co-Director of the NIH Training Grant in Biomolecular Technology at UC Davis, an innovative multidisciplinary research and educational training for doctoral students working at the interface of life sciences and engineering/physical sciences in application areas related to human health and wellness. From 2006-2013, I was the PI and Director of the NSF CREATE-IGERT, an interdisciplinary graduate training program focused on applications of plant biotechnology to biopharmaceuticals, biorefineries and sustainable agriculture. At the undergraduate level I teach courses in Biotechnology Facility Design and Regulatory Compliance as well as Engineering Economics and our Capstone Design Course for our Biochemical Engineering major (a separate ABET accredited major which I helped to establish in 1994). I teach the biochemical engineering courses related to biomanufacturing facility design and technoeconomic modeling as well as bioreactor design and analysis and the bioprocess engineering laboratory. My research has generated over 70 referred journal articles, five issued patents and two additional patent applications in the area of plant-based expression of recombinant proteins, with practical applications in human therapeutics, subunit vaccines, biodefense agents and biomaterials for medical applications. I have also had training in methods to analyze and develop sustainable, scalable business models for commercialization of ideas, techniques and processes generated from engineering research through my participation in NSF I-Corps, National Collegiate Inventors and Innovators Alliance, an NSF STTR project, the UC Davis Entrepreneurship Academy and the UC Davis Engineering Technology Translation Center. In 2013 I cofounded Inserogen, Inc. with Dr. Lucas Arzola, a former PhD student whose doctoral work focused on transient production of biodefense agents and animal vaccines in plant systems. My formal training in chemical and biochemical engineering combined with my research experience in plant made pharmaceuticals, teaching experience in bioprocess engineering, engineering economics and technoeconomic modeling, and entrepreneurship training are well suited to my role in the proposed project.

B. Positions and Honors

Positions and Employment

1979-1982	Member of Tech. Staff	Sandia National Laboratories, Livermore, CA
1982-1985	Research Assistant	Chemical Engineering, University of Maryland, College Park, MD
1985-1993	Assistant Professor	Chemical Engineering, University of California, Davis, CA
1993-1998	Associate Professor	Chemical Engr. & Mat. Sci., University of California, Davis, CA
1998-present	Professor	Chemical Engr. & Mat. Sci., University of California, Davis, CA
2000-2001	Acting Associate Dean	College of Engineering, University of California, Davis, CA
2001-2013	Associate Dean	College of Engineering, University of California, Davis, CA
2013- present	Faculty Director	UC Davis NSF ADVANCE Program, Davis, CA

Honors

UC Davis College of Engineering Innovator, 2014
Visiting Professor of Beijing University of Chemical Technology, July 2013
Outstanding Service Award, UC Extension, 2010
Outstanding Volunteer Award, For Inspiration and Recognition of Science and Technology, Sacramento Regional, 2004
Outstanding Chemical Engineering Professor, AIChE Student Chapter, Davis, CA, 1992
Best Presentation of Session, American Control Conference, Atlanta, GA, 1988
Faculty Development Award, University of California, Davis, CA, 1988
Graduate Research Incentive Fellowship, University of Maryland, College Park, MD, 1982
Sandia One Year on Campus Program, University of California, Berkeley, CA, 1979-80
Graduated With Distinction, Stanford University, 1979
Standard Oil Engineering Scholarship, Stanford, CA, 1978
Hazel Lagerson Scholarship, University of California, Davis, CA, 1976

C. Contributions to Science

1) Inducible Plant Viral Expression Systems. There is an urgent need in the biotechnology industry for fast, flexible and cost-effective biomanufacturing platforms to meet the growing demand for safe, affordable therapeutics, particularly as biosimilars and biogenerics come on-line and as markets expand globally. Historically, one of the major limitations of plant and plant cell culture production systems is the low yield of recombinant protein (typically on the order of 1-10 mg/L for cell culture systems and <0.5% of total soluble protein in plant tissues). To address this challenge, my collaborators and I developed a novel plant-based expression system that uses the inherent ability of plant viral RNA to replicate rapidly to a high copy number within compatible plant hosts, enabling greater recombinant protein production per cell. This expression system, called **CMViva** for ***C****ucumber* ***M****osaic* ***V****irus* **i**nducible **v**iral **a**mplicon, has been used for high level expression of heterologous proteins in whole plants using transient agroinfiltration as well as transgenic plant cell suspension cultures. The CMViva expression system utilizes agrobacterium-mediated transformation to introduce the foreign gene into the plant host. We have genetically engineered the *Agrobacterium tumefaciens* Ti plasmid to contain *modified* complementary DNAs (cDNAs) representing the complete genome of *Cucumber mosaic virus* (CMV), in which the CMV coat protein gene has been replaced by our target (*e.g.* product) gene, which along with other modifications, ensure that infectious CMV virus is not generated. Furthermore, because one of the key CMV-encoded proteins, a primary component of the viral replicase, is under the control of a tightly regulated chemically-inducible promoter, the recombinant viral amplicons are only produced intracellularly in the agroinfected cells when the chemical inducer is applied. We have also included sequences coding for a secretion signal peptide upstream of our transgene to provide targeting of the product to the extracellular space to facilitate product recovery. Although it was technically quite challenging due to the number of different system components and large size of the resulting DNA vector, our team succeeded in integrating the entire CMV amplicon expression system on a *single* binary expression vector (~27.4kb). Although different bacteria are able to infect (and transfer T-DNA) to the same plant cell, by incorporating all of the expression components on a single plasmid we are able to ensure that an infected cell will contain *all* of the necessary components. Another particularly appealing aspect of the CMViva expression system is that it can be used in stably transformed plants and/or transgenic plant cell suspension cultures (since the viral amplicon is dormant until activated by the chemical inducer) for long-term production of a recombinant protein. It should also be pointed out that plant viruses are considered safe as they do not replicate in mammals or vertebrates

and, as a common component in human and animal food sources, are considered non-toxic by the EPA. In addition, because CMV is a plant virus with one of the broadest host ranges, the expression system can be used in many different plant species allowing great flexibility. The impact of this work has been the development of an inducible viral amplicon expression system that can be used for high level recombinant protein production using a variety of plant hosts and formats (transient, stable transgenic plants, stable transgenic plant cell cultures in bioreactors). My role on the project was in concept development, writing the proposal that funded the project and serving as the PI, mentoring, directing and supervising the graduate students who performed the production and process optimization work, data analysis and interpretation, and editing/revising the manuscripts.

a) Mysore R. Sudarshana, Michael A. Plesha, Sandra Uratsu, Bryce W. Falk, Abhaya M. Dandekar, Ting-Kuo Huang, Karen A. McDonald, "A Chemically Inducible Cucumber mosaic virus Amplicon System for Expression of Heterologous Proteins in Plant Tissues" Plant Biotechnology Journal, 4: 551-559 (2006).
b) Michael A. Plesha, Ting-Kuo Huang, Abhaya M. Dandekar, Bryce W. Falk and Karen A. McDonald, "High-Level Transient Production of a Heterologous Protein in Plants by Optimizing Induction of a Chemically Inducible Viral Amplicon Expression System", Biotechnology Progress, 23(6): 1277-1285 (2007).
c) Michael A. Plesha, Ting-Kuo Huang, Abhaya M. Dandekar, Bryce W. Falk, and Karen A. McDonald, "Optimization of the Bioprocessing Conditions for Scale-Up of Transient Production of a Heterologous Protein in Plants Using a Chemically Inducible Viral Amplicon Expression System", Biotechnology Progress, 25(3): 722-734 (2009).
d) Min Sook Hwang, Benjamin E. Lindenmuth, Karen A. McDonald and Bryce W. Falk, "Bipartite and tripartite Cucumber mosaic virus-based vectors for producing the *Acidothermus cellulolyticus* endo-1,4-beta-glucanase and other proteins in non-transgenic plants", BMC Biotechnology, 12:66 (2012).

2) Semicontinuous Plant Cell Bioreactor Systems. The use of transgenic plant cell cultures for production of recombinant proteins is an emerging field (the first FDA approved biologic, Elelyso™, produced in carrot cell culture by Protalix Biotherapeutics and Pfizer, Inc. for treatment of Gaucher disease was approved in May 2012). Plants do not harbor or propagate mammalian viruses/pathogens, grow on simple chemically defined media and have the ability to perform complex post-translational modifications. One of the challenges of large scale production of recombinant proteins using plant cell cultures in bioreactors is due to the slow growth rate of plant cells and therefore the long time frames and extensive inoculum seed train required. Our group has focused on processes in which the plant cells can be kept in the bioreactor (with efficient secretion of the product into the culture medium and methods for maintaining product stability) and reused in a semicontinuous or perfusion operation instead of traditional batch or fed-batch operations. In addition, we have developed bioreactor based processes for efficient, long-term semi-continuous production of heterologous proteins using plant cell cultures based on metabolically regulated expression systems or chemically inducible expression systems. The latter papers are the first, to our knowledge, to describe a continuous process for production of a recombinant protein in transgenic plant cell cultures utilizing an inducible viral amplicon system. The impact of this work is the demonstration of long term, semicontinuous operation allowing for high specific productivities, reduced downtime (turnaround time) and potential to conform to cGMP requirements. My role on the project was in designing the experiments, writing the proposal that funded the project and serving as the PI, mentoring, directing and supervising the graduate students who performed the bioreactor work, data analysis and interpretation, and editing/revising the manuscripts.

a) Melody M. Trexler, Karen A. McDonald and Alan P. Jackman, "A Cyclical Semicontinuous Process for Production of Human α_1-Antitrypsin Using Metabolically Induced Plant Cell Suspension Cultures", Biotechnology Progress, 21: 321 - 328 (2005).
b) Karen A. McDonald, Lo Ming Hong, David M. Trombly, Qing Xie and Alan P. Jackman, "Production of Human α-1-Antitrypsin from Transgenic Rice Cell Culture in a Membrane Bioreactor", Biotechnology Progress 21: 728-734 (2005).
c) Ting-Kuo Huang, Michael A. Plesha, and Karen A. McDonald, "Semicontinuous Bioreactor Production of a Recombinant Human Therapeutic Protein Using a Chemically Inducible Viral Amplicon Expression System in Transgenic Plant Cell Suspension Culture", Biotechnology and Bioengineering, 106(3): 408-421 (2010).

d) Corbin, J.M., Kailemia, M.J., Cadieux, C.L., Alkanaimsh, S., Karuppanan, K., Rodriguez, R.L., Lebrilla, C.B., Cerasoli, D.M., McDonald, K.A. and Nandi, S. (2018). Purification, Characterization, and N-glycosylation of Recombinant Butyrylcholinesterase from Transgenic Rice Cell Suspension Cultures, *Biotechnology and Bioengineering* (*In press*).

3) Technoeconomic Modeling and Analysis of Plant-Based Production Systems. There have been very few published reports describing the capital investment required and annual production costs for biomanufacturing facilities that utilize alternative production hosts. These analyses provide a more rigorous manufacturing cost analyses based on designing and sizing unit operations and performing material and energy balances as well as scheduling batch processes. The models indicate that plant produced therapeutics and even industrial enzymes can lower cost of goods compared with alternative approaches. Several of these models were developed in collaboration with industry colleagues (indicated by * below) to provide realistic process operations and parameters for industrial scale biomanufacturing facilities. My role on the projects was to define the scope and design premises for the model, either supervising graduate students and/or undergraduates in developing the model using SuperPro Designer, or in some cases developing the model myself, reviewing all aspects of the model, and drafting or editing the manuscript or poster.

a) Elizabeth Zapalac and Karen A. McDonald, "Economic and Environmental Assessment of the Purification of Alpha-1-Antitrypsin from Transgenic Plant Cell Suspension Cultures. In *Development of Sustainable Bioprocesses - Modeling and Assessment*, Eds.; Heinzle, E.; Biwer, A., Wiley (2007).
b) Daniel Tusé*, Tiffany Tu, and Karen A. McDonald, "Manufacturing Economics of Plant-Made Biologics: Case Studies in Therapeutic and Industrial Enzymes," BioMed Research International, vol. 2014, Article ID 256135, 16 pages, 2014. doi:10.1155/2014/256135 (2014).
c) Somen Nandi, Aaron T. Kwong, Barry R. Holtz*, Robert L. Erwin*, Sylvain Marcel*, and Karen A. McDonald, "Techno-economic analysis of a transient plant-based platform for monoclonal antibody production," *mAbs*, 00-00. doi: 10.1080/19420862.2016.1227901 (2016).
d) Matthew J. McNulty, Yuri Gleba*, Daniel Tusé*, Somen Nandi and Karen A. McDonald, "Technoeconomic analysis of a plant-based platform for manufacturing food safety antimicrobials," Poster Presentation, Plant-Based Vaccines, Antibodies and Biologics, Albuferia, Portugal, June 5-7 (2017).

Refereed Journal Articles in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1Vizs7v4qlTkR/bibliography/52894208/public/?sort=date&direction=ascending

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

Current and Recent Research Support

NSF
NSF, UC Davis ADVANCE: Institutional Transformation to Build and Sustain a Diverse Community of Innovative STEM Scholars
Programs for recruitment, retention and promotion of women STEM faculty
Role: Co-PI

DTRA
Glycan Modulation of Pharmaceutical Glycoproteins by *In Vitro* Enzymatic Approaches
Impact of glycosylation on plant-made bioscavengers for biodefense applications
Role: PI

NSF
Preparing Engineering Graduate Students for the 21st Century
A graduate training program to help diversify our engineering graduate programs
Role: Co-PI

USAID
Developing Climate-Resistant Plant-Based Recombinant Subunit Vaccine Against Foot and Mouth Disease Virus of Livestock

A research project to develop an edible feed to deliver a FMDV vaccine to cattle
Role: Co-PI

UC Davis Innovation Institute for Food and Health
Technoeconomic Analysis of Plant-Made Endolysins for Food Safety
Development of a technoeconomic model of a facility for making recombinant endolysins in spinach
Role: PI

NASA
Center for the Utilization of Biological Engineering in Space (CUBES)
Systems engineering for sustainable, regenerable processes to provide food, fuel, pharmaceuticals and materials required to sustain life in a resource limited deep space environment such as Mars
Role: Co-PI and UC Davis Lead

T32 GM 08799
NIH-NIGMS, Training Program in Biomolecular Technology
An interdisciplinary graduate training program in biotechnology
Role: Co-Director

Leidos, Inc. Grant
Leidos, Inc., Rice Cell Culture Production of Butyrylcholinesterase
Development of a transgenic rice cell suspension bioreactor system for production of butyrylcholinesterase, a bioscavenger for organophosphate nerve agents
Role: PI

NSF
Novel Bioreactor-Based Systems for Producing Ebola Monoclonal Antibodies in *Nicotiana benthamiana* Plant Cell Suspension Culture
Development of a plant cell bioreactor system for production of ZMapp monoclonal antibodies
Role: PI

Alpha-1 Foundation
In Vitro Evaluation of a Plant-Made Alpha-1-Antitrypsin
Analysis of neutrophil elastase inhibition of plant-made AAT, comparison with human plasma derived AAT
Role: PI

NSF PFI
Plant Based Manufacturing of Orphan Drug Human Biobetter Alpha-1-Antitrypsin
Process development for purification of plant based production of alpha-1 antitrypsin for treatment of lung disease
Role: PI