BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Altin, John Andrew

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

POSITION TITLE: Assistant 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	Completion Date MM/YYYY	FIELD OF STUDY
Australian National University (ANU)	PhB(Hons)	12/2006	Biochemistry/ Molecular Biology
ANU	LLB(Hons)	12/2007	Law
ANU	PhD	12/2012	Immunology/Genetics

A. PERSONAL STATEMENT

I graduated from the Australian National University and then undertook PhD training in molecular and cellular immunology in the immunogenomics lab of Prof Chris Goodnow. My research used genome-wide mutagenesis to elucidate 3 novel molecular and cellular pathways that regulate the helper T cell response (Altin JA *et al* 2011; Altin JA *et al* 2012; Altin *et al* 2014), and was recognized as the most outstanding thesis submitted within the Institute that year.

After my PhD, I joined Prognosys Biosciences, a start-up biotech company founded by Dr Mark Chee (co-founder of Illumina Inc) to develop immunological applications for novel, highly-multiplexed proteomics and genomics assays that utilize next generation sequencing. There, I led an interdisciplinary team to develop novel technologies that enable highly-multiplexed analysis of peptide binding to immunological ligands (patents: US-10288608-B2, WO-2014145047-A1, WO-2012139110-A2). In 2017, I joined the faculty at TGen, where I lead an interdisciplinary research team specializing in Immunology and Genomics. Among a number of other projects, my research program includes the lead or co-lead role on 3 NIAID-supported projects that develop and apply assays to study T and B cell responses to pathogens at genome-scale.

B. POSITIONS AND HONORS

Positions and Employment

2012-2014 Scientist I and II, Applications Development, Prognosys Biosciences

2014-2017 Senior Scientist, Applications Development, Prognosys Biosciences

2017-present Assistant Professor, Translational Genomics Research Institute

Service and Professional Memberships

2010-2012 Treasurer, Australasian Society for Immunology – ACT Branch

2010-2012 Advisor of 2 students in the Biochemistry and Molecular Biology Honours Program, ANU (each undertook a year-long research-intensive project)

2019-2021 American Association of Immunology

Honors

2006 University Medal (Biochemistry & Molecular Biology), ANU

2007 University Medal (Law), ANU

2008-2012 ANU Vice-Chancellor's PhD Scholar (top ranked student)

2013 Fenner Medal for most outstanding PhD thesis in immunology, ANU

2013 Milne Prize for most outstanding PhD thesis at JCSMR Institute

C. CONTRIBUTION TO SCIENCE

A full list of my published work can be found here:
https://www.ncbi.nlm.nih.gov/myncbi/john.altin.1/bibliography/public/

1. Genetic basis of CD4 T cell regulation and differentiation. The activation and differentiation of T cells represents a central event in the immune response, and its genetic dysregulation underlies pathologies including immunodeficiency, autoimmunity and allergy. I contributed to a number of studies (including **a** and **d** below) that implicated novel genetic variants in different genes (*Ndfip1*, *Card11*) in the regulation of T cell expansion and differentiation. I was the primary driver of experimental design, analysis and writing in these 2 studies. I was also primarily responsible for a project that identified a novel subset of helper T cells with inhibitory function (**b**), and designed experiments and analyzed data in a collaborative study that demonstrated differential control of helper T cell differentiation states by regulatory T cells (**c**). Together, these studies contribute novel molecular and cellular mechanisms to our understanding of how different types of T cell responses arise and are regulated.

a. **Altin JA**, Daley SR, Howitt J, Rickards HJ, Batkin AK, Horikawa K, Prasad SJ, Nelms KA, Kumar S, Wu LC, Tan SS, Cook MC, Goodnow CC. Ndfip1 mediates peripheral tolerance to self and exogenous antigen by inducing cell cycle exit in responding CD4+ T cells. Proc Natl Acad Sci U S A. 2014, 111(6):2067-74. PMCID: PMC3926078

b. **Altin JA**, Goodnow CC, Cook MC. IL-10+ CTLA-4+ Th2 inhibitory cells form in a Foxp3-independent, IL-2-dependent manner from Th2 effectors during chronic inflammation. J Immunol. 2012, 88:5478-88. PMID: 22547705

c. Tian L, **Altin JA**, Makaroff LM, Cook MC, Goodnow CC, Dooley J, Liston A. Foxp3+ regulatory T cells exert asymmetric control over helper responses by inducing Th2 cell apoptosis. Blood. 2011, 118(7):1845-53. PMCID: PMC3158716

d. **Altin JA**, Tian L, Liston A, Bertram EM, Goodnow CC, Cook MC. Decreased T-cell receptor signaling through CARD11 differentially compromises forkhead box protein 3-positive regulatory versus T(H)2 effector cells to cause allergy. J Allergy Clin Immunol. 2011, 127(5):1277-85. PMCID: PMC3189857

2. Multiplexed genomic assay development. As a Senior Applications Scientist at Prognosys Biosciences, I led a team that developed immunological applications for a novel assay platform ('PepSeq') capable of assaying >10^5 programmable peptides for binding to immunological ligands – disclosed in the patents described below (**a.** and **b.**) Prior to the advent of this technology, no similar platform existed to enable comprehensive analysis of antibody responses at this scale per cost. The PepSeq platform is poised to enable a new approach to the study of systems immunology.

a. **Altin JA**, Chee MS. (2014) Methods for detecting peptide/MHC/TCR binding, WO-2014145047-A1.

b. Kozlov IA, **Altin JA**, Capek P, Chee MS. (2014) Polynucleotide conjugates and methods for analyte detection, US-10288608-B2.

3. High-resolution analysis of adaptive immune responses to pathogens at genome-scale. As an Assistant Professor at TGen, I lead projects that develop and apply assays to study B and T cell responses to pathogens at a systems-level. Using the PepSeq technology described above, we have developed a fully-in-vitro assay for highly-multiplexed virome-wide analysis of antibodies at high resolution (supported by U24AI152172, role: PI). We have used this system to define signatures of SARS-CoV-2 exposure, and shown that the response to the pandemic virus includes cross-reactive antibodies that recognize epitopes in Spike S2 that have conserved homologs in prior endemic coronaviruses (**a** below). In addition, we have developed highly-multiplexed peptide:MHC class II assays and used these to enable genome-scale T cell epitope discovery. This tool has been coupled with deep transcriptional phenotyping by single cell sequencing and used to study the T cell response to *Mycobacterium Tuberculosis* (supported by R21AI149311 & AI152564, role: MPI).

a. Ladner JT, Henson SN … Chee MS, Shiryaev SA, **Altin JA**. Epitope-resolved profiling of the SARS-CoV-2 antibody response identifies cross-reactivity with endemic human coronaviruses. 2021, Cell Reports Medicine 2(1):10089. PMCID:PMC7816965.

D. RESEARCH SUPPORT

1U24AI152172-01 (Altin) 04/10/2020 – 03/31/2025
NIAID
A scalable platform for highly-multiplexed analysis of antibody reactivity form <1ul of blood
This project aims to develop a technology that enables antibodies against 100,000s of custom targets to be profiled simultaneously and cost-effectively using a drop of blood, with a focus on antibodies that recognize any of the >300 viruses capable of infecting humans.
Role: PI

U24 Administrative Supplement (Altin) 05/01/2020-4/30/2022
NIAID
The goal of this supplement is to extend the highly-multiplexed peptide-based platform for deep serological analysis developed in the parent U24 to SARS-CoV-2.
Role: PI

1 R21 AI149311-01 (Altin/Ernst) 02/18/2020 – 01/31/2022
NIAID
A novel approach for deep phenotyping the CD4 T cell response to Mycobacterium Tuberculosis
The major goal of this project is to identify signatures differentially associated with progression and nonprogression to active TB by analyzing the breadth and diversity of antigen recognition and T cell signatures.
Role: MPI

1 R21 AI152564-01 (Ernst/Altin) 09/01/2020 – 08/30/2022
NIAID
Host genetic diversity, T cell responses, and outcomes of TB
This project will study the basis of improved control of Mtb infection in particular strains of Collaborative Cross mice using a number of tools, including deep, antigen-resolved single cell sequencing of responding T cells.
Role: MPI

2018 Collab in Oncology Grant (Altin/Askar/Reynolds) 03/01/19 – 11/28/2021
Baylor Scott & White Research Institute (BSWRI) and Translational Genomics Research Institute (TGen) Collaboration in Oncology Research *Applying a novel, highly-multiplexed proteomics assay to predict alloimmunity*
The goal of this project is to perform a comprehensive empirical HLA class II binding analysis of HLA-derived peptides, in order to predict the number of allopeptides in any given allogeneic stem cell transplantation donor:recipient pair, and therefore the risk of graft-versus-host disease.
Role: MPI

California Institute for Regenerative Medicine (CIRM) (Zaia) 05/01/20 – 04/30/2021
Evaluation of SARS-CO-V-2 Antibody in Convalescent Volunteer Plasma Donors: A CIRM Testing Center
The goal of this project is to establish a testing center to enable the qualification of plasma from convalescent COVID-19 donors, and additionally to use a range of serological assays to discover correlates of the plasma's clinical efficacy.
Role: Subaward PI

NCI P30 CA033572 SARS-CoV-2 Administrative Supplement 05/01/20 – 04/30/2021
Evaluation of SARS-Co-V-2 Immunoglobulins for Prevention or Treatment of COVID-19
The goal of this project is to identify biomarkers of convalescent plasma potency in COVID-19 patients.
Role: Subaward PI

Contract W15QKN209C003 (Keim) 01/01/20 – 12/31/2021
DTRA (Sub Northern Arizona University)
Small molecule screening to identify high-affinity interactions for the development of prototype Bartonella henselae and Chikungunya virus biothreat detectors based upon small molecule moieties.
The goal of this project is to identify small molecules with high affinity for the pathogen target proteins (Task 1) and then deploy them in a Lateral Flow Assay format (Task 2).
Role: Subaward PI

ADHS 17-00007403 (Keim) 04/01/18 – 03/31/2021
ABRC (Sub Northern Arizona University)
Discovery of Coccidioides epitopes that stimulate adaptive T-cell responses for diagnostic assay development
Goal: We are using a highly-muliplexed peptide:MHC binding assay to screen the Cocci proteome for visibility to the human T cell response. Identification of novel T cell targets against this pathogen may enable new diagnostic strategies and may inform vaccine design.

Role: Subaward PI