



## STEPHEN ALBERT JOHNSTON

Director, Center for Innovations in Medicine  
Biodesign Institute  
Professor School of Life Sciences  
Arizona State University

P.O Box 875901  
Tempe, AZ 85287-5901  
480-727-0792  
Stephen.johnston@asu.edu

### Education

1975 University of Wisconsin-Madison, B.S. (Molecular Biology)  
1976-1981 University of Wisconsin-Madison, Ph.Ds.  
(Genetics/Biochemistry) and (Plant Genetics/Plant Breeding)  
1981-1983 The Pennsylvania State University Medical Center  
Postdoctoral (Biochemistry)

### Research and Professional Experience

2005-Present Director, Center for Innovations in Medicine, Biodesign Institute,  
Professor SOLS, Arizona State University  
2007- 2012 Director of the Biological Design PhD Program at The Biodesign  
Institute, Arizona State University  
2006-2009 Member of Biodesign Institute Directorate, Arizona State University  
1999-2005 Professor of Microbiology, UTSW  
1998-2005 Director, Center for Biomedical Inventions, UTSW  
1995-2005 Professor of Internal Medicine, UTSW  
1995-2000 Professor of Biochemistry, UTSW  
1993-2005 Eugene Tragus Chair in Molecular Cardiology, UTSW  
1991/1995 Associate Professor, Internal Medicine and  
Biochemistry, University of Texas-Southwestern  
Medical Center  
1989-1990 Associate Professor of Biology and Biochemical  
Engineering, Duke  
1989-1990 Duke University (Research Career Development Award)  
1984-1989 Assistant Professor of Biology and Biochemical  
Engineering, Duke University  
1982-1983 NIH Postdoctoral Fellow, Department of Biochemistry, The  
Pennsylvania State University Medical Center (with Dr. James E.  
Hopper), Research: The isolation and characterization of the *GAL4*  
regulatory gene of yeast.  
1981-1982 Rockefeller Postdoctoral Fellow (with Dr. James E. Hopper)

1975-1981 Graduate Student, Department of Genetics (with Dr. Oliver E. Nelson) and Program in Plant Breeding/Plant Genetics (with Dr. Robert E. Hanneman), University of Wisconsin-Madison. Thesis Title: *The Role and Nature of Genic Balance in Endosperm Development.*

### **Major Service:**

1997-2013 BioChem 20/20 Advisory Committee of Experts (ACE) for Defense Intelligent Agency (Founding member)

2003- 2013 SAB of Western Regional Center of Excellence for Biodefense and Emerging Infectious Diseases

2004- Present Member, Institute of Medicine Forum on Microbial Threats

2009- 2012 Integration Panel, DoD Breast Cancer Program

2011- Present Scientific Advisory Council, Beckman Foundation

2018 – Present Member, National Academy of Inventors

### **Companies Started::**

Eliance. Merged to Macrogenics, Inc.

Synbody Biotechnology Inc. (terminated)

HealthTell, Inc.

Calviri, Inc.

### **Major Scientific Accomplishments:**

**EBN** 1982: Endosperm Balance Number Hypothesis (*Science*). New concept in how genomes are imprinted to explain interspecific crossing barriers. Widely used now in making new hybrid plants.

**GAL 4** 1982: Cloning of Gal4 (*PNAS*). First eukaryotic regulator cloned (done by Ray Gestland's lab at same time). Established the regulatory protein has dosage effect (had been argued that they would not). Used dosage effect to argue that Gal4 was poised

on the promoter in the uninduced state (contrary to existing model and now know to be the case).

**PDR** 1985: Pathogen-derived resistance (PDR) (*J. of Theoretical Biology*, with John Sanford). Proposed that genes of virus could be manipulated to confer resistance in host. The concept was renamed “intracellular immunization” 3 years later by David Baltimore. This technology is now used to make some commercial plants and bacteria stocks resistant to viral infection.

1986-7: C-terminus of Gal4 required for gene activation and interaction with negative regulator, Gal80. (*PNAS, Cell*). The discovery of functional domains in Gal4 was actually done in 1984 while I was in Hoppers lab .

**CAP-INDEPENDENT IN VITRO TRANSLATION** 1986: With Bill Dougherty developed the use of potyvirus mimic for cap-independent in vitro mammalian translation. This technique is widely used in systems now

**FIRST ORGANELLE TRANSFORMATION** 1988: Mitochondrial Transformation (*Science*, with John Sanford and Ron Butow). Demonstrated the first transformation of an organelle. This technology is now widely used for mitochondria and chloroplast transformation.

1989 DNA binding specificity of Gal4 zinc-finger is conferred outside of zinc-finger. (*Nature*, also discovered by Chambon group at same time). This was the first definition of how the DNA binding specificity of zinc fingers is conferred.

**GENE GUN** 1991. Gene gun. (*Technique*, with John Sanford). Development of the helium gene gun. This device is commercially available and widely used for plant transformation and genetic vaccination of animals.

**IN VIVO ANIMAL TRANSFORMATION** 1991. Direct transformation of tissue in living mice with gene gun. (*PNAS*, with Sandy Williams and John Sanford). This report and the one of Wolff et al were the first of direct transformation of tissues in an animal.

**GENE VACCINES** 1992. Genetic Immunization (*Nature*). This was first demonstration that introduction of simple plasmids encoding antigens could elicit an immune response. This was revolutionary approach to immunization and vaccines. It is in phase II and III clinical trials and approved for several animal vaccines.

1992. Sug genes affect transcription. (*Nature*). This was the first publication on sequence of Sug1 and its control on transcription and identification as ATPase. First AAA protein.

1993. Structure function studies of Gal4 activation domain. (*Cell*, with Tom Kodadek). This was one of the first indications that ADs are not simply acid amphipathic helices.

**TEV PROTEASE** 1993. With Bill Dougherty invented the TEV protease system. This protease is now widely used and arguably the best in the field.

1994-1998. Discovery, crystal structure and activities of Bleomycin hydrolase. (*JBC, Science and Cell*, with Lemoor Joshua-Tor). We discovered this cysteine protease and delineated its unusual features including the ability to act as a carboxypeptidase, aminopeptidase and peptide ligase. This work revived work on this protein.

1995. Sug1 directly interacts with the AD of Gal4 and thyroid receptor (*Nature*, with David Moore). This was the demonstration that Sug1 directly interacted with the Gal4 AD and was associated with transcription factors. We later corrected that sug 1 was also in the proteasome. This made most of the field associate transcriptional effects as through the proteolytic effects of the proteasome. The field has turned around on this point after years of uphill battle.

**EXPRESSION LIBRARY IMMUNIZATION** 1995. Expression Library Immunization. (*Nature*). This was the demonstration of a technique to unbiasedly test all the genes of a pathogen for their ability to protect against infection. It was the first genomic approach to vaccine discovery. Also the first demonstration of genetic immunization protecting against bacterial infection.

**PHAGE PANNING ON CELLS/CELL TARGETING PEPTIDES** 1996. Selection of peptide-presenting bacteriophage that bind and transfect mammalian cells (*Nature Medicine*). This was the first demonstration of selection of peptides on cells that targeted uptake. Variations on this approach are widely used now.

**CBI** 1998. Started Center for Biomedical Inventions (with Tom Kodadek, Skip Garner, Sandy Williams and Bob Meidell). This was the first center of this type. It was dedicated to inventing blue-sky solutions to basic biomedical problems and reducing to practice with highly interdisciplinary approaches.

**BioSignature Diagnostics:** 1998. Introduced concept biosignature diagnostics (with Shaun Jones, DARPA) with idea of transforming diagnostics to personal normalized signatures. Emphasis on presymptomatic diagnosis.

**LINEAR EXPRESSION ELEMENTS** 1999. Linear expression elements. (*Nature Biotechnology*, with Kathy Sykes). A new method to functionally test genes and promoters in cells or animals without cloning was demonstrated. Basis for a company and widely used now.

1999. A non-proteolytic requirement for the 19S in nucleotide excision repair. (*Mol. Cell*, with Errol Friedberg). This was the first evidence that the 19S regulatory subunit of the proteasome was required for a cellular function that did not involve proteolysis.

2001. Evidence that the 19S subunit of the proteasome is required for transcriptional elongation. (*Mol. Cell*, with Tom Kodadek). This was the key report to link the proteasome to transcription in a mode other than degradation.

2002. Gal4 recruits a subunit of the proteasome to the promoter on induction. (*Science*, with Tom Kodadek). This report was the first evidence that the proteasome units function independently in vivo and that recruitment of the new APIS complex was an early event in transcription.

**HTP ANTIBODY PRODUCTION** 2004. High through put antibody production. (*Nature Biotech*). We created a system for the rapid transition of genome sequence into antibodies against the corresponding protein. Over 3,000 antibodies made and widely used. Commercialized with Abcam.

**IN VIVO PATHOGEN MICROARRAYS** 2004. Analysis of gene expression in the pathogen during infection. (*PNAS* with Rick Lyons). We developed several techniques that allowed us for the first time to analyze the global gene expression patterns of a pathogen in vivo during the course of infection.

**IMMUNOSIGNATURING DIAGNOSTICS:** At UTSW first developed the concept of signaturing the antibodies or T-cells to determine the health status of people. At ASU with Phil Stafford developed the peptide array technology to measure immunosignaturing and demonstrated its effectiveness. This technology is licensed to HealthTell, an ASU spinoff.

**SYNBODIES:** With Chris Diehnelt and Neal Woodbury developed synbodies as a simple method to make small, chemically synthesized antibody like molecules for research, therapeutics and anti-infectives. This technology was licensed to Synbody Biotechnology, an ASU spinoff.

**UNIVERSAL PROPHYLACTIC CANCER VACCINE:** Created a simple approach to making a potentially universal preventative cancer vaccine. Now a national initiative (Artemis Project) supported by the National Breast Cancer Initiative.

## **Publications**

Shen L, Zhao Zhan-Gong, Lainson J, Brown J, Sykes K, Johnston SA, Diehnelt C.  
“Production of high-complexity frameshift neoantigen peptide microarrays”. RSC Advances. 11 Aug 2020. DOI: 10.1039/d0ra05267a

Peterson M, Murphy SN, Lainson J, Zhang J, Shen L, Diehnelt CW, Johnston SA.  
“Cancer-type specific vaccine based on shared frameshift neoantigens effectively treats breast cancer in a murine model”. BMC Immunology. 2020 May 5:21 (1):25 doi: 10.1186/s12865-020-00350-3.

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- Shen, L, Zhang J, Lee H, Batista M, Johnston SA. "RNA Transcription and Splicing Errors as a Source of Cancer Frameshift Neoantigens for Vaccines". *Scientific Reports*; 2019 Oct 2; PMID: 31578439
- Wang L, Stafford P, Johnston SA. "A common antibody response is induced by a wide variety of human pathogens". (in review). 2018
- Zhang J, Shen L, Johnston SA. "Using Frameshift Peptide Arrays for Cancer Neo-Antigens Screening". *Sci Rep*. 2018 Nov 26;8(1) PMID: 30478295
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## Patents and Licenses (selected of ~50)

1. Linear and circular expression elements. Patents and Licensed (S.A. Johnston/K. Sykes, co-inventors)
2. Rationally designed and chemically synthesized promoter for genetic vaccine and gene therapy (B. Qu, co-inventor) (pending)
3. Methods and compositions for vaccination comprising nucleic acid and/or polypeptide sequences of the genus *Borrelia* (Lyme Disease) (K. Sykes, K. Stemke-Hale, co-inventors) (filed)
4. Use of Parapox B2L Protein to Modify Immune Responses to Administered Antigens (M. McGuire, co-inventor) (patented)
5. Methods and compositions for vaccination comprising nucleic acid and/or polypeptide sequences of chlamydia. (filed)
6. Methods and compositions for vaccination comprising nucleic acid and/or polypeptide sequences of chlamydia psittaci. (K. Sykes, K. Stemke-Hale and B. Kaltenboeck co-inventors) (filed)
7. Methods for vaccine identification and compositions for vaccination comprising nucleic acid and/or polypeptide sequences of the herpesvirus family. (filed)

8. Methods for rapid and efficient protein-crosslinking. (T. Kodadek and D. Fancy, co-inventors) (patented)
9. A new high throughput DNA synthesizer based on masks. (E. Livesay and S. Liu, co-inventors) (pending)
10. Expression library immunization. (W. Lai and M. Barry, co-inventors) (patented & licensed)
11. A simple system for purifying authentic proteins and peptides (William Dougherty, co-inventor) (patented & licensed)
12. Genetic immunization as a simple and improved method for eliciting an immune response (John Sanford, co-inventor) (pending & licensed)
13. An improved biolistic device (J. Sanford and M. Devit, co-inventors) (patented & licensed). This is for the helium device sold by BioRad.
14. A method for isolating protease encoding genes. (Bruce Kohorn, co-inventor) (licensed)
15. Parasite-derived resistance (John Sanford, co-inventor) (patented)
16. Amyloid  $\beta$  Gene Vaccines (Roger Rosenberg and Bao-Xi Qu, co-inventors) (patented)
17. Particle-mediated transformation of vertebrate tissue cells (John Sanford, co-inventor) (patented)
18. Use of parapox PP30 protein to modify immune responses to administered antigens (patented)
19. Nucleic acid and polypeptide sequences useful as adjuvants (patented)
20. Particle-mediated bombardment of DNA sequences into tissue to induce an immune response (patented)
21. E. coli resistance to Q $\beta$  virus infection (patented)
22. Method and apparatus for introducing biological substances into living cells (patented)
23. Methods and Compositions for Vaccination Comprising Nucleic Sequences of *Chlamydia psittaci*. U.S. Patent application: No. 09/738,269. PCT application: No. 10/023,437 US patent Issued 2010. Inventors: B. Kaltenboeck, K. Sykes, K. Stemke-Hale, S. Johnston
24. Methods and Compositions for Vaccination Comprising Nucleic Acid and/or Polypeptide Sequences of *Chlamydia*. US Patent No. 8,298,542 B2. Date of patent: Oct. 30, 2012. Inventors: S. Johnston, K. Stemke-Hale, K. Sykes, B. Kaltenboeck.
25. Immobilizing an Entity in a Desired Orientation on a Support Material. US Patent No. 8,481,679 B2. Date of patent July 9, 2013. Inventors: SA Johnston, CW Diehnelt.
26. Peptide array quality control. US Patent No. 10006919. Date of Patent: June 26, 2018. Inventors: Neal Woodbury, SA Johnston, Phillip Stafford.
27. Systems and methods of epitope binning and antibody profiling. US Patent No. 10,900,975. Date of Patent: January 26, 2021. Inventors: Stephen Albert Johnston.
28. Peptide array quality control. US Patent No. 11,067,582. Date of Patent: July 20, 2021. Inventors: Neal Woodbury, Stephen Albert Johnston, Phillip Stafford.