BIOGRAPHICAL SKETCH

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NAME: Alexander Eckehart Urban

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

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Freie Universitaet Berlin, Germany	B.Sc. (equiv.)	1996	Biochemistry
Yale University, New Haven, CT	M.A.	2002	Mol., Cell. And Dev. Bio.
Yale University, New Haven, CT	Ph.D.	2007	Mol., Cell. And Dev. Bio.

A. Personal Statement

I have well over 15 years of experience in developing and applying high-throughput and high-resolution genomics analysis tools and procedures, in particular in the context of studying genomic sequence variation in brain development and function. I have been involved on numerous occasions in using a large-scale and high-throughput setup for genomics analyses as well as carrying out analyses over several levels of genomics and epigenomics information. This includes for example participation in the ENCODE and 1000 Genomes projects and also in the Brain Somatic Mosaicism Network (BSMN) consortium project. I have experience with developing and applying state-of-the-art and emerging genomics and epigenomics technologies for the analysis of gene expression, genomic DNA sequence and structure, DNA methylation and chromatin modification, in human cells and human cell culture systems, including stem cell culture models. For example I was co-first author of the paper in Science (Korbel, Urban, Affourtit et al., 2007, PMID 17901297) on developing next-generation-sequencing based paired-end mapping of CNVs and SVs, an approach that is now a standard part of whole-human-genome sequencing projects and also a critical component of advanced RNA-Seq approaches and the study of long-range chromatin interactions. Two main, and connected, directions of research in my laboratory are the investigation of the molecular effects of large genome sequence variants during neuronal development using iPSC model systems and the study of the nature and effects of somatic genome variation using tissue culture models and primary tissue samples. I have been mentoring multiple students and postdoctoral fellows since starting my own laboratory and, for example, the first of these postdoctoral fellows just started her own tenure-track faculty position.

B. Positions and Honors

Positions & Employment

February 2008 – April 2010: Postdoctoral Associate, Yale University School of Medicine, Deparment of Genetics

Since April 2010: Assistant Professor, Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, and Department of Genetics; Member, Stanford Center for Genomics and Personalized Medicine, and Program in Genetics of Brain Function

Honors

2008 John Spangler Nicholas Prize
2012 NARSAD Young Investigator Award

2012 NIH Director's New Innovator Award
2013 Stanford Psychiatry Department Award for Advancing Science
2016 Tashia and John Morgridge Faculty Scholar, Stanford Child Health Research Institute

C. Contributions to Science

(**these authors contributed equally or ‡are co-corresponding authors*)

1) Developed high-resolution array technology for discovery and fine-mapping of benign and pathogenic CNVs. CNVs could only be mapped with very low resolution. We increased mapping resolution by several orders of magnitude, in the process we determined for the first time the exact breakpoint in an (atypical) case of 22q11-Deletion-Syndrome and increased by several fold the resolution for partial-trisomy-21 breakpoints; high-density oligomer array CGH is today the standard first-line method in clinical cytogenetics.

a) **Urban AE***, Korbel JO*, Selzer R, Richmond T, Hacker A, Popescu GV, Cubells JF, Green R, Emanuel BS, Gerstein MB, Weissman SM‡, Snyder M‡. High-resolution mapping of DNA copy alterations in human chromosome 22 using high-density tiling oligonucleotide arrays. ***Proc Natl Acad Sci U S A***. 2006 Mar 21;103(12):4534-9. PMID: 16537408
b) Korbel JO*, **Urban AE***, Grubert F, Du J, Royce TE, Starr P, Zhong G, Emanuel BS, Weissman SM, Snyder M, Gerstein MB. Systematic prediction and validation of breakpoints associated with copy-number variants in the human genome. ***Proc Natl Acad Sci U S A***. 2007 Jun 12;104(24):10110-5. PMID: 17551006
c) Korbel JO*, Tirosh-Wagner T*, **Urban AE***, Chen XN, Kasowski M, Dai L, Grubert F, Erdman C, … , Warburton D, Weissman S, Gerstein MB, Snyder M‡, Korenberg JR‡. The genetic architecture of Down syndrome phenotypes revealed by high-resolution analysis of human segmental trisomies. ***Proc Natl Acad Sci U S A***. 2009 Jul 21;106(29):12031-6. Epub 2009 Jul 13. PMID: 19597142
d) Haraksingh RR, Abyzov AA, **Urban AE**. Comprehensive performance comparison of high-resolution array platforms for genome-wide CNV analysis in humans. ***BMC Genomics***. 2017 Apr 24;18(1):321. PMID: 28438122

2) Developed next-generation-sequencing based paired-end mapping and read-depth analysis of the human genome sequence. Massively-parallel ("next-generation") sequencing platforms had just become available and we developed two basic procedures to use them in the genome-wide analysis of CNV and SV – i.e. paired-end mapping (PEM) and read-depth analysis (RDA). We demonstrated the power of PEM by detecting large numbers of SVs in normal genomes; both methods are now standard components of human whole-genome sequencing and for example were used by the 1000 Genomes Project to which we were standing contributors.

a) Korbel JO*, **Urban AE***, Affourtit JP*, Godwin B, Grubert F, Simons JF, Kim PM, Palejev D, Carriero NJ, Du L, Taillon BE, Chen Z, Tanzer A, Saunders AC, Chi J, Yang F, Carter NP, Hurles ME, Weissman SM, Harkins TT, Gerstein MB, Egholm M‡, Snyder M‡. Paired-end mapping reveals extensive structural variation in the human genome. ***Science***. 2007 Oct 19;318(5849):420-6. Epub 2007 Sep 27. PMID: 17901297
b) Abyzov A, **Urban AE**, Snyder M, Gerstein M. CNVnator: An approach to characterize and genotype atypical CNVs using high-throughput sequencing coupled with population and family structure. ***Genome Research***. 2011 Apr 14. [Epub ahead of print] PMID: 21324876
c) 1000 Genomes Project Consortium[1], Durbin RM, Abecasis GR, Altshuler DL, Auton A, Brooks LD, Durbin RM, Gibbs RA, Hurles ME, McVean GA. A map of human genome variation from population scale sequencing. ***Nature***. 2010 Oct 28;467(7319):1050-1. PMID: 20981092
[1] The 1000 Genomes Project had more than 540 co-authors, with only the writing teams being listed in the short format references; Dr. Urban is a co-author as a member of both the analytical and structural variation groups of the 1000 Genomes Consortium.
d) Zhou B*, Arthur JG*, Pattni R, Ho SS, Wong WH‡, **Urban AE‡**. Deep sequencing with multiple strategies unlocks the Venter/HuRef genome as reference for genomics tools development and benchmarking. ***Scientific Data.*** 2018 Dec 18;5:180261. PMID: 30561434

3) Developed and advanced genomics and epigenomics analysis methods on cutting-edge platforms.
I have contributed to the development or improvement of advanced methods for genomics and epigenomics analysis, at each time based on the most cutting-edge array and sequencing platforms.

a) Stewart D, Kural D, Strömberg MP, Lee W-P, Walker J, Konkel M, Stütz AM, **Urban AE**, Grubert G, Lam HYK, Batzer M, Korbel JO, Huff C, Xing J, Marth G, and the 1000 Genomes Project. Comprehensive discovery and characterization of mobile element insertions from the 1000 Genomes Pilot Project data. ***PLoS Genet****.* 2011 Aug;7(8):e1002236. PMID: 21876680
b) Zhou B, Ho S, Zhang X, Pattni R, Haraksingh RR, Abyzov A, **Urban AE**. Whole-genome sequencing analysis of genomic copy number variation (CNV) using low-coverage and paired-end strategies is highly efficient and outperforms array based CNV analysis. ***J Med Genetics***. 2018 Nov;55(11):735-743. PMID: 30061371
c) Zhou B, Ho S, Zhu X, Zhang X, Spies N, Byeon S, Arthur JG, Pattni R, Ben-Efraim N, Haney MS, Haraksingh RR, Song G, Perrin D, Wong WH, Abyzov A, **Urban AE**. Comprehensive, Integrated, and Phased Whole-Genome Analysis of the Primary ENCODE Cell Line K562. ***Genome Research.*** *In press*.
d) Zhou B, Ho S, Greer SU, Spies N, Bell JM, Zhu X, Zhang X, Byeon S, Arthur JG, Pattni R, Ben-Efraim N, Huang Y, Song G, Perrin D, Wong WH, Abyzov A, **Urban AE**. Haplotype-resolved and integrated genome analysis of the cancer cell line HepG2. ***Nucleic Acids Research.*** *In press.*

4) Multilevel and integrated genomics and epigenomics analyses. I am frequently using cutting edge genomics and epigenomics methods in an integrative fashion, i.e. combining data across multiple levels of genomic and epigenomic information and control. For example, using this approach we recently discovered that large CNVs that are strongly associated with neuropsychiatric disorders, and specifically the large deletion on chromosome 22q11, can affect chromatin states and chromosome folding patterns not just locally and directly but also globally and indirectly across the cell's nucleus.

a) ENCODE Project Consortium[1]. Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project. ***Nature****.* 2007 Jun 14;447(7146):799-816. PMID: 17571346
[1] The ENCODE Consortium, during its pilot phase, had initially more than 200 members who were contributing various types of experimental and/or analytical work to the project, including Dr. Urban as a member of the microarray group at Yale, and who are listed as co-authors in the full publications.
b) Kasowski M*, Grubert F*, Heffelfinger C, Hariharan M, Asabere A, Waszak SM, Habegger L, Rozowsky J, Shi M, **Urban AE**, …, Weissman SM, Gerstein MB, Korbel JO‡, Snyder M‡. Variation in transcription factor binding among humans. ***Science****.* 2010 Apr 9;328(5975):232-5. PMID: 20299548
c) Li J*, Shi M*, Ma Z*, Zhao S, Euskirchen G, Ziskin J, **Urban AE**, Hallmayer JF, Snyder MP. Integrated Systems Analysis Reveals A Molecular Network Underlying Autism Spectrum Disorders. ***Molecular Systems Biology****.* 2014 Dec 30;10(12):774. PMID: 25549968
d) Zhang X*, Zhang Y*, Zhu X*, Purmann C, Haney MS, Ward TR, Yao J, Weissman SM, **Urban AE**. Local and global chromatin interactions are altered by large genomic deletions associated with human brain development. ***Nature Communications.*** 2018 Dec 17;9(1): 5356. PMID 30559385

5) Genome variation in somatic tissues and stem cell model systems.
The emerging genomics platforms enable us for the first time to comprehensively detect and study the presence and effects of CNVs and retrotranspositions as somatic variants, in stem cell systems, primary tissues and in a combination of these tissues. We have developed and established novel approaches to harness the full potential of the genomics platforms in combination with these model systems and tissues.

a) Abyzov A, Mariani J*, Palejev D*, Zhang Y*, Haney MS*, Tomasini L*, Rosenberg-Belmaker L, Ferrandino A, Wilson M, Grigorenko EL, Huttner A, Weissman SM, **Urban AE‡**, Gerstein M‡, Vaccarino FM‡. Somatic copy number mosaicism in human skin revealed by induced pluripotent stem cells. ***Nature***. 2012 Dec 20; 492(7429):438-42. doi: 10.1038/nature11629. Epub 2012 Nov 18. PMID: 23160490
b) Abyzov A, Tomasini L, Zhou B, Vasmatzis N, Coppola G, Amenduni M, Pattni R, Wilson M, Gerstein M, Weissman M, **Urban AE**, Vaccarino F. One thousand somatic SNVs per skin fibroblast cell set baseline of mosaic mutational load with patterns that suggest proliferative origin. ***Genome Research****.* 2017 Feb.

PMID: 28235832

c) McConnell M*, Moran JV*, Abyzov A, Akbarian S, Bae T, Erwin JA, Fasching L, Flasch DA, Freed D, Ganz J, Kwan KY, …, Weinberger DR, **Urban AE**, Gage FH, Lehner T, Senthil G, Walsh C, Chess A, Courchesne E, Gleeson JG, Kidd JM, Park PJ, Pevsner J, Vaccarino FM, Brain Somatic Mosaicism Network. Intersection of diverse neuronal genomes and neuropsychiatric disease: the Brain Somatic Mosaicism Network. ***Science***. 2017 Apr 28;356(6336). PMID: 28450582

d) Bae T, Tomasini L, Mariani J, Zhou B, Roychowdhury T, Franjic D, Pletikos M, Pattni R, Chen BJ, Venturini E, Riley-Gillis B, Sestan N, **Urban AE**, Abyzov A‡, Vaccarino FM‡. Different mutational rates and mechanisms in human cells at pregastrulation and neurogenesis. ***Science***. 2017 Dec 7. pii: eaan8690. doi: 10.1126/science.aan8690. [Epub ahead of print]. PMID: 29217587

(**these authors contributed equally or* ‡*are co-corresponding authors*)

Full list of published work on MyBibliography (NCBI):
https://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/44935252/
(above: 20 publications selected from 58 publications)

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

Ongoing Research Support:

U01 (MH106876-01) 04/01/2015 – 03/31/2020
Somatic Mosaicism in the Brain of Tourette Syndrome (Brain Somatic Mosaicism Network, BSMN)
Using postmortem brain tissue, in this proposal we investigate the extent of somatic genomic mosaicism in cells of the brains of individuals with Tourette Syndrome (TS) and matched controls.
Role: Subcontract-PI. PI: Flora Vaccarino (Yale)

R01 (MH100900-01) 09/01/13 – 08/31/18 (in no-cost extension)
Integrative Molecular and Phenotype Analysis of 22q11.2 Deletion Syndrome
Convert skin cells from 40 patients with 22q11Deletion Syndrome into iPSC and from there into neurons. Characterize the functioning of these neurons and the associated gene expression networks.
Role: Co-Investigator. PI: Joachim Hallmayer

P50 (HG007735-01) 04/01/2014 – 03/31/2019
Center for Excellence in Genomic Science (CEGS): Center for Personal Dynamic Regulomes
Use a transposase-based method for genome-wide analysis of open chromatin states. Map the interactions of lncRNAs with chromatin, DNA methylation sites, and high order chromosome interactions.
Role: Co-Investigator/Project Director. PI: Howard Chang

U19 (MH104172-01) 04/01/2014 – 03/31/2019
Multimodal analysis of high-risk psychosis mutations in induced neuronal cells
Screen pharmacological compounds for activity in psychotic disorders using induced neurons from iPS cells with schizophrenia-associated mutations such as CNVs in 22q11 and 16p11 and characterize their cellular phenotypes.
Role: Co-Investigator. MPI: Levinson, Südhof, Wernig

Tashia and John Morgridge Faculty Scholar Award 09/01/2016 – 08/31/2019
Stanford Child Health Research Institute
A transgenic marmoset model for neurodevelopmental disorders
Create transgenic marmosets with large CNVs in their genomes that are syntenic to large CNVs in humans that are associated with neurodevelopmental, neuropsychiatric disorders such as autism and schizophrenia.
Role: PI

SFARI Research Award 09/01/2016 – 08/31/2019
Simons Foundation Autism Research Initiative
Somatic mosaicism in autism spectrum disorders
Explore the role of somatic genome variation in ASD.

Role: Subcontract-PI, MPI: Vaccarino (Yale) and Abyzov (Mayo)

Completed Research Support (Past 3 Years):

National Ataxia Foundation Young Investigator Award 12/31/2013 – 12/30/2014
Genomic and epigenomic analyses in an induced pluripotent stem cell model of ADCA-DN
Role: PI

Brain and Behavior Research Foundation Type: YI Award (19673) 2/01/13 – 12/31/2014
NARSAD 2012 Young Investigator Award. Integrated genomics analysis of iPSC, neuronal precursors and neurons from patients with Velocardiofacial Syndrome (VCFS)
Role: PI

R01 EUREKA (MH094740-01) 07/01/2011 – 04/30/2017
Testing the Hypothesis of Somatic Cell Retrotransposition in Human Brain
Role: Co-Investigator. PI: Douglas F. Levinson

R01 (MH096262-01A1) 08/13/12 – 04/30/2017
HLA and schizophrenia: a high-throughput sequencing study
Role: Co-Investigator. PI: Douglas F. Levinson

March of Dimes Foundation Research Grant (#6-FY13-142) 06/01/2013 – 05/31/2017
March of Dimes Research Grant. Multilevel genomics analyses of models of neuronal and cardiovascular symptoms in 22q11-Deletion-Syndrome using induced pluripotent stem cells
Role: PI

DP2 (MH100010-01) 09/30/2012 – 08/31/2017
Director's New Innovator Award. Genomic and epigenomic effects of large CNVs in neurons from iPSC
Role: PI

Stanford Neurosciences Institute (SNI) Seed Grant (SG1-09) 09/01/2015 – 10/31/2017
Creating a transgenic monkey model of autism
Role: MPI (with Karen Parker)

Stanford Medicine Faculty Innovation Program Grant 03/01/2016 – 02/28/2018
A new standard procedure for chromosome analysis
Role: PI

R21 (HD083629-01) 04/01/2015 – 03/31/2018
Epigenetic regulation of social impairments and treatment response in autism
Role: Co-Investigator. PI: Karen Parker

R01 (MH100914-01A1) 09/01/2013 – 12/31/2018
Genomic mosaicism in the developing human brain
Role: Subcontract-PI. MPI: Flora Vaccarino, Nenad Sestan, Mark Gerstein (Yale)