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: 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 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 considerable numbers of students and postdoctoral fellows since starting my own laboratory and, for example, the first of these postdoctoral fellows just started on 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

Full list of published work by MyBibliography (NCBI):
http://www.ncbi.nlm.nih.gov/sites/myncbi/alexander.urban.2/bibliography/44935252/public/?sort=date&direction=ascending. (below: 24 publications selected from 47 publications)
(**these authors contributed equally* *or* ‡*are co-corresponding authors*)**

a) 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 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.

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

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

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

Haraksingh R, Abyzov A, Gerstein M, **Urban AE**, Snyder M. Genome-wide mapping of Copy Number Variation in humans: comparative analysis of high resolution of array platforms. *PLoS One*.
2011 Nov; 6(11):e27859. Epub 2011 Nov 30. PMID: 22140474

Haraksingh RR, Abyzov AA, **Urban AE**. Comprehensive performance comparison of high-resolution array platforms for genome-wide CNV analysis in humans. *BMC Genomics. In Press.*

b) 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.

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

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 Res.* 2011 Apr 14. [Epub ahead of print] PMID: 21324876

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 pilot phase studies 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.

Mills RE*, Walter K*, Stewart C*, Handsaker RE*, Chen K*, Alkan C*, Abyzov A*, Yoon SC*, Ye K*, Cheetham RK, Chinwalla A, Conrad DF, Fu Y, Grubert F, Hajirasouliha I, Hormozdiari F, … , **Urban AE**, Walker JA, Wu J, Zhang Y, Zhang ZD, Batzer MA, Ding L, Marth GT, McVean G, Sebat J, Snyder M, Wang J, Ye K, Eichler EE‡, Gerstein MB‡, Hurles ME‡, Lee C‡, McCarroll SA‡, Korbel JO‡ & the 1000 Genomes Project. Mapping structural variation at fine scale by population-scale genome sequencing. *Nature.* 2011 Feb 3;470:59-65. PMID: 21293372

c) Developed and advanced genomics and epigenomics analysis methods on cutting-edge platforms. I have consistently 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.

Bertone P*, Stolc V*, Royce TE, Rozowsky JS, **Urban AE**, Zhu X, Rinn JL, Tongprasit W, Samanta M, Weissman S, Gerstein M‡, Snyder M‡. Global identification of human transcribed sequences with genome tiling arrays. *Science.* 2004 Dec 24;306(5705):2242-6.

Pelizzola M*, Koga Y*, **Urban AE**, Krauthammer M, Weissman S, Halaban R, Molinaro AM. MEDME: An experimental and analytical methodology for the estimation of DNA methylation levels based on microarray derived MeDIP-enrichment. *Genome Res.* 2008 Sep 2. [Epub ahead of print] PMCID: PMC2556264

Pan X, **Urban AE**, Palejev D, Schulz V, Grubert F, Hu Y, Snyder M, Weissman SM. A procedure for highly specific, sensitive and unbiased whole-genome amplification. *Proc Natl Acad Sci U S A.* 2008 Oct 7;105(40):15499-504.

Battle A, Mostafavi S, Zhu X, Potash JB, Weissman MM, McCormick C, Haudenschild CD, Beckman KB, Shi J, Mei R, **Urban AE**, Montgomery SB, Levinson DF, and Koller D. Characterizing the Genetic Basis of Transcriptome Diversity through RNA-Sequencing of 922 Individuals. *Genome Res.* 2014 Jan;24(1):14-24.

d) 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.

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.
[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.

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

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.

Li J*, Ma Z*, Shi M*, Malty RH, Aoki H, Minic Z, Phanse S, Jin K, Wall DP, Zhang Z, **Urban AE**, Hallmayer J, Babu M‡, Snyder M‡. Identification of human neuronal protein complexes reveals biochemical activities and convergent mechanisms of action in Autism Spectrum Disorders. *Cell Syst.* 2015 Nov 25;1(5):361-374.

Zhang Y*, Zhang X*, Zhou X*, Purmann C, Haney MS, Ward T, Yao X, Weissman SM‡, **Urban AE‡**. Local and global chromatin interactions are altered by large genomic deletions associated with human brain development. *Submitted.*

e) Copy number variation and retrotransposition 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.

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.

O'Huallachain M, Karczewski KJ, Weissman SM, **Urban AE**, Snyder MP.
Extensive genetic variation in somatic human tissues. *Proc Natl Acad Sci U S A*. 2012 Oct 30;109(44):18018-23.

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

Urban AE and Purmann C. Using iPSCs and genomics to catch CNVs in the act. *Nature Genetics.* 2015 Feb; 47(2):100-1.

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. 2*017 Feb 24

McConnell M*, Moran JV*, Abyzov A, Akbarian S, Bae T, Erwin JA, Fasching L, Flasch DA, Freed D, Ganz J, Kwan KY, Kwon M, Lodato MA, Paquola ACM, Rodin R, Rosenbluh C, Sestan N, Sherman MA, Song S, Straub R, Jeremy Thorpe, 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. In Press.*

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

D. Research Support

Ongoing:
Director's New Innovator Award. Genomic and epigenomic effects of large CNVs in neurons from iPSC
Role: PI. Agency: NIMH.

Type: DP2 (MH100010-01). 09/30/2012 – 08/31/2017.
Integrate multiple levels of genomic and epigenomic analysis (genome sequence, DNA methylation, chromatin states and conformations, gene expression patterns) over the course of cellular differentiation in multiple iPSC lines from patients with large genomic CNVs and neurodevelopmental, neuropsychiatric disorders.

Testing the Hypothesis of Somatic Cell Retrotransposition in Human Brain
Role: Co-Investigator. PI: Douglas F. Levinson. Agency: NIMH
Type: R01 EUREKA (MH094740-01). 07/01/2011 – 04/30/2017 (no-cost extension).
Determine whether somatic genomic mosaicism in human brains is involved in the etiology of schizophrenia by using deep whole-genome sequencing of DNA samples from human brain and bioinformatics analyses.

Genomic mosaicism in the developing human brain
Role: Subcontract-PI. MPI: Flora Vaccarino, Nenad Sestan, Mark Gerstein (Yale U.). NIMH
Type: R01 (MH100914-01A1). 09/01/2013 – 08/31/2018.
Analyze the genomes of subpopulations of cells of the developing brain for structural sequence changes. This may play a role in normal development and individual susceptibility to neuropsychiatric disorders.

HLA and schizophrenia: a high-throughput sequencing study
Role: Co-Investigator. PI: Douglas F. Levinson. Agency: NIMH.
Type: R01 (MH096262-01A1). 08/13/12 – 04/30/2017 (no-cost extension).
Determine which HLA genotypes are associated with schizophrenia, in a very large cohort.

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. Funder: March of Dimes Foundation.
Type: Research Grant (#6-FY13-142). 06/01/2013 – 05/31/2017 (no-cost extension).
Differentiate iPSCs with deletions in 22q11 into cell lineages relevant to cardiovascular development and functioning, assay the effects of the 22q11 genomic deletion across multiple levels of control and regulation.

Somatic Mosaicism in the Brain of Tourette Syndrome (Brain Somatic Mosaicism Network, BSMN)
Role: Subcontract-PI. PI: Flora Vaccarino (Yale U.). Agency: NIMH
Type: U01 (MH106876-01). 04/01/2015 – 03/31/2020.
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.

Integrative Molecular and Phenotype Analysis of 22q11.2 Deletion Syndrome
Role: Co-Investigator. PI: Joachim Hallmayer. Agency: NIMH
Type: R01 (MH100900-01). 09/01/13 – 08/31/18.
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.

Center for Excellence in Genomic Science (CEGS): Center for Personal Dynamic Regulomes
Role: Co-Investigator/Project Director. PI: Howard Chang. Agency: NHGRI
Type: P50 (HG007735-01). 04/01/2014 – 03/31/2019.
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.

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

Epigenetic regulation of social impairments and treatment response in autism
Role: Co-Investigator. PI: Karen Parker. Agency: NICHD
Type: R21 (HD083629-01). 04/01/2015 – 03/31/2017.
Investigate DNA methylation of oxytocin receptors and arginine-vasopressin receptors and its relation to social impairment and treatment response in autism spectrum disorder (ASD).

Creating a transgenic monkey model of autism
Role: Co-PI (with Karen Parker). Funder: Stanford Neurosciences Institute (SNI)
Type: SNI Seed Grant (SG1-09). 09/01/2015 – 08/31/2017.
Use various genome-editing methods in marmoset stem cells to create transgenic marmosets with large CNVs in their genomes that are syntenic to large CNVs in humans that are associated with autism.

A new standard procedure for chromosome analysis
Role: PI. Funder: Stanford Medicine Faculty Innovation Program.

Type: Faculty Innovation Program Grant. 03/01/2016 – 02/28/2018.
Establish experimental and computational workflows that make it possible to use next-generation DNA sequencing technology for routine clinical cytogenetics use and analysis of complex genome rearrangements.

A transgenic marmoset model for neurodevelopmental disorders
Role: PI. Funder: Stanford Child Health Research Institute.
Type: Tashia and John Morgridge Faculty Scholar Award. 09/01/2016 – 08/31/2019.
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. The transgenic marmosets will be used to identify biomarkers and inform pharmacological interventions.

Completed:

Whole-genome sequencing of Velocardiofacial Syndrome – finding the genetic modifiers.
Role: PI. Funder: Stanford Pediatric Research Fund
Type: Category I Award – Pilot Early Career (UL1 RR025744). 4/01/11 – 3/31/12.

Using patient-derived iPS cells to identify cellular defects in DiGeorge Syndrome
Role: Co-I. PI: Ricardo Dolmetsch. Funder: Johnson&Johnson Foundation and Stanford Institute for Neuro-Innovation and Translational Science, 5/01/2011 – 4/30/2012.

Depression susceptibility genes and networks: expression, eQTL and GWAS analysis.
Role: Co-I. PI: Douglas F. Levinson. Agency: NIMH. Type: RC2 (1RC2MH089916-01). 9/30/09 - 8/31/12.

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

NARSAD 2012 Young Investigator Award. Integrated genomics analysis of iPSC, neuronal precursors and neurons from patients with Velocardiofacial Syndrome (VCFS)
Role: PI. Funder: Brain and Behavior Research Foundation. Type: YI Award (19673). 2/01/13 – 12/31/14.