

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
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NAME Robert Martin Plenge	POSITION TITLE <i>Assistant Professor (Harvard Medical School) Director, Genetics and Genomics (BWH, Division of Rheumatology, Immunology and Allergy) Associate Member (Broad Institute, Inc.)</i>		
eRA COMMONS USER NAME RPLENGE			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of California, San Diego (UCSD)	B.S.	1988-1992	Biology ( <i>cum laude</i> )
Case Western Reserve University (CWRU)	Ph.D., M.D.	1992-2000	Human Genetics
University of California, San Francisco (UCSF)		2000-2002	Internal Medicine
Harvard Medical School (HMS) and Brigham and Women's Hospital (BWH)		2002-2006	Clinical Rheumatology
Broad Institute of MIT and Harvard		2003-2008	Human Genetics

### A. PERSONAL STATEMENT

For the current project, I will use my expertise in performing functional studies of the CD40 rheumatoid arthritis (RA) risk allele and high-throughput drug screens. Dysregulation of the immune system is a fundamental disease mechanism, yet is incompletely understood. My laboratory applies human genetics and genomics tools to understand dysregulation of the immune system in the context of human disease [and rheumatoid arthritis (RA) in particular]. Our ultimate goal is to improve the lives of patients with immune-mediated diseases. Towards this end, my laboratory has three key research areas: (1) Discovery genetics/genomics: we use genome-wide approaches (genotyping and sequencing) to find DNA variants that are associated with immune-mediated traits, including disease susceptibility, response to therapy, and subclinical immune phenotypes (e.g., inflammation, autoantibody production); (2) Functional translation: once associated DNA variants are discovered, we use "humans as the model organism" to understand function and key biological pathways, with a long-term goal of disease prevention and drug discovery; we use genomic discoveries to guide high-throughput, small molecule drug screens; and (3) Clinical translation: we use clinical data from the electronic medical records (EMR) linked with biospecimens to enable clinical translational research.

### B. POSITIONS AND HONORS

#### Positions and Employment

1994-1995 Howard Hughes Medical Student Fellow (CWRU, advisor = Dr. Huntington Willard)  
1995-2000 Medical Scientist Training Program (CWRU, advisor = Dr. Huntington Willard)  
2000-2002 Internal Medicine Resident, Department of Medicine (UCSF)  
2002-2006 Clinical Rheumatology Fellow, Division of Rheumatology, Immunology and Allergy (BWH)  
2003-2008 Post-doctoral Research Fellow, Broad Institute of MIT and Harvard (Dr. David Altshuler)  
2006-2008 Instructor of Medicine, Division of Rheumatology, Immunology and Allergy (BWH)  
2008-current Assistant Professor of Medicine, Division of Rheumatology, Immunology and Allergy (BWH)  
2008-current Director, Genetics and Genomics, Division of Rheumatology, Immunology and Allergy (BWH)  
2011-current Associate Member, Broad Institute of MIT and Harvard

#### Other Experience and Professional Memberships

2000-2002 Molecular Medicine Research Fellowship Program (UCSF)  
2002-current Massachusetts Medical License  
2004-current Internal Medicine Board Certification  
2006-current Rheumatology Board Certification  
2007-2012 Editorial Board, *Arthritis Research and Therapy*  
2011-2012 Advisory Editor, *Arthritis & Rheumatism*  
2012-current Associate Editor, *Arthritis & Rheumatism*

- 2012-current Scientific Advisory Council, Research and Education Foundation of the ACR
- 2003-current Ad hoc manuscript reviewer: *Nature*, *New England Journal of Medicine*, *Nature Genetics*, *JAMA*, *PLoS Genetics*, *Am. Journal of Human Genetics*, *Arth & Rheum* and >15 other journals
- 2009-current Ad hoc grant reviewer: NIH Genetics of Human Disease (GHD) Study Section, Psoriasis Foundation, American College of Rheumatology “*Within Our Reach*” campaign, Alliance for Lupus Research, EULAR “*Orphan Disease Program*”, and other.

### **Selected Honors and Awards**

- 1992 Phi Beta Delta International Honor Society (UCSD)
- 1995 Alpha Omega Alpha Research Award (CWRU)
- 1995 Pre-doctoral Clinical Award, The American Society of Human Genetics
- 2007, 2008 Excellence in Tutoring Award, Human Genetics (HMS)
- 2008 Young Investigator Award, Department of Medicine (BWH)
- 2008-current Burroughs Wellcome Fund Career Award for Medical Scientists
- 2012 Member, The American Society for Clinical Investigation

### **C. SELECTED PEER-REVIEWED PUBLICATIONS (from >70 PubMed references)**

#### **Most relevant to the current application**

1. **Plenge RM\***, Seielstad M\*, Padyukov L, Lee AT, Remmers EF, Ding B, Liew A, Khalili H, Chandrasekaran A, Davies LRL, Li W, Tan AKS, Bonnard C, Ong RTH, Thalamuthu A, Pettersson S, Liu C, Tian C, Chen WV, Carulli J, Altshuler D, Alfredsson L, Criswell LA, Amos CI, Seldin MF, W, Kastner DA, Klareskog L\*, and Gregersen PK\*. (2007) *Genome-Wide Search Identifies TRAF1-C5 as Rheumatoid Arthritis Risk Locus*, *New Eng J Med*. Vol. 357 (12): 1199-209. \*contributed equally. PMID: PMC2636867
2. **Plenge RM**, Cotsapas C, Davies L, Price AL, et al (2007) *Two independent alleles at 6q23 associated with risk of rheumatoid arthritis*, *Nat Genet*. Vol 39 (12): 1477-82. PMID: PMC2652744
3. Raychaudhuri S, Remmers EF, Lee AT, Hackett R, Guiducci C, ... Klareskog L, Gregersen PK, Daly MJ, **Plenge RM** (2008) *Common variants at CD40 and other loci confer risk of rheumatoid arthritis*. *Nat Genet*, 40(10):1216-23. PMID: PMC2757650
4. Stahl EA, Raychaudhuri S, Remmers EF, Xie G, Eyre S, Thomson BP, ... Gregersen PK, Klareskog L, **Plenge RM** (2010) *Genome-wide association study meta-analysis identifies seven new rheumatoid arthritis risk loci*. *Nat Genet* 42(6):508-14. PMC Journal – In Process.
5. Stahl EA, Wegmann D, Kraft P, Chen R, Kallberg H, Kurreeman FAS, Gregersen PK, Alfredsson L, Siminovitch KA, Worthington K, de Bakker PIW, Raychaudhuri S\*, **Plenge RM\*** (2012) *Bayesian inference reveals polygenic architecture of four common disease*, *Nat Genet*. Mar 25. doi: PMID: 22446960

#### **Additional recent publications of importance to the field (in chronological order)**

1. **Plenge RM**, Hendrich BD, Schwartz C, Arena JF, Naumova A, Sapienza C, Winter RM, Willard HF (1997) *A promoter mutation in the XIST gene in two unrelated families with skewed X chromosome inactivation*, *Nat Genet* Vol. 17: 353-356. PMID: 9354806
2. **Plenge RM**, Padyukov L, Remmers EF, et al, (2005) *Replication of putative candidate gene associations with rheumatoid arthritis in over 4,000 samples from North America and Sweden: association of susceptibility with PTPN22, CTLA4 and PADI4*, *Am J Hum Genet* Vol. 77: 1044-1060. PMID: PMC1285162
3. Remmers EF\*, **Plenge RM\***, Lee AT, Graham RR, Hom G, Behrens TW, de Bakker PIW, Le JM, Lee H, Batliwalla F, Li W, Masters SL, Booty MG, Carulli JP, Padyukov L, Alfredsson L, Klareskog L, Chen WV, Amos CI, Criswell LA, Seldin MF, Kastner DL, and Gregersen PK (2007) *STAT4 and the risk of rheumatoid arthritis and systemic lupus erythematosus*, *New Eng J Med*. Vol. 357 (10): 977-86. \*contributed equally. PMID: PMC2630215
4. Raychaudhuri S, **Plenge RM**, Rossin EJ, Ng AC; International Schizophrenia Consortium, Purcell SM, Sklar P, Scolnick EM, Xavier RJ, Altshuler D, Daly MJ (2009) *Identifying Relationships Among Genomic Disease Regions: Predicting Genes at Pathogenic SNP Associations and Rare Deletions*. *PLoS Genetics* 5(6):e1000534. [Epub 2009 Jun 26] PMID: PMC2694358

5. Raychaudhuri S, Thomson BP, Remmers EF, Eyre S, Hinks A, Guiducci C, Catanese JJ, Xie G, Stahl EA, ... **Plenge RM** (2009) *Genetic variants at CD28, PRDM1, and CD2/CD58 are associated with rheumatoid arthritis risk.* Nat Genet 41(12):1313-8. PMID: PMC3142887
6. Karlson EW, Chibnik LB, Kraft P, Cui J, Keenan BT, Ding B, Raychaudhuri S, Klareskog L, Alfredsson L, Plenge RM (2010) *Cumulative association of 22 genetic variants with seropositive rheumatoid arthritis risk.* Ann Rheum Dis 69(6):1077-85. PMID: PMC2933175
7. Cui J, Saevarsdottir S, Thomson B, Padyukov L, van der Helm-van Mil AH, Nititham J, Hughes LB, de Vries N, ... **Plenge RM** (2010) *Rheumatoid arthritis risk allele PTPRC is also associated with response to anti-tumor necrosis factor alpha therapy.* Arthritis Rheum 62(7):1849-6. PMC Journal – In Process.
8. Liao KP, Cai T, Gainer V, Goryachev S, Zeng-Treitler Q, Raychaudhuri S, Szolovits P, Churchill S, Murphy S, Kohane I, Karlson EW, **Plenge RM** (2010) *Electronic medical records for discovery research in rheumatoid arthritis.* Arthritis Care Res (Hoboken) 62(8): 1120–1127. PMID: PMC3121049
9. Zhernakova A, Stahl EA, Trynka G, Raychaudhuri S, Festen EA, Franke L, Westra HJ, Fehrmann RS, Kurreeman FA, Thomson B, Gupta N, Romanos J, ...Huizinga TW, Wijmenga C, **Plenge RM** (2011) *Meta-analysis of genome-wide association studies in celiac disease and rheumatoid arthritis identifies fourteen non-HLA shared loci.* PLoS Genet. Feb;7(2):e1002004. [Epub 2011 Feb 24.] PMID: PMC3044685
10. Kurreeman F, Liao K, Chibnik L, Hickey B, Stahl E, Gainer V, Li G, Bry L, Mahan S, Ardlie K, Thomson B, Szolovits P, Churchill S, Murphy SN, Cai T, Raychaudhuri S, Kohane I, Karlson E, **Plenge RM** (2011) *Genetic Basis of Autoantibody Positive and Negative Rheumatoid Arthritis Risk in a Multi-ethnic Cohort Derived from Electronic Health Records,* Am J Hum Genet. Jan 7;88(1):57-69. PMID: PMC3014362

#### D. RESEARCH SUPPORT

##### Ongoing Research Support

Career Award for Medical Scientists Plenge (PI) 9/01/2008-8/31/2013

Burroughs Wellcome Fund

Genotype-phenotype studies of rheumatoid arthritis susceptibility genes

*Goal: Career development award to facilitate the transition to an independent investigator; the research pertains to genotype-phenotype correlations of rheumatoid arthritis susceptibility genes*

R01 AR056291 Choi (PI) 8/01/2008-7/31/2013

NIH-NIAMS

Genetics of Gout

*Goal: Conduct a GWAS of uric acid and gout, incorporating environmental risk factors.*

Role: co-investigator

R01 AR056768 Plenge (PI) 5/15/2009-4/30/2014

NIH-NIAMS

Dissection of two rheumatoid arthritis risk loci from genome-wide studies

*Goal: Sequence two RA risk loci (TRAF1-C5 and TNFAIP3) for common and rare variants, and to conduct pilot functional studies of the risk alleles*

U01 GM092691 Plenge (PI) 7/01/2010-6/30/2015

NIH-NIGMS

Genetic predictors of response to anti-TNF therapy in rheumatoid arthritis

*Goal: GWAS genotype new samples and develop new statistical methodologies for analysis of response to anti-TNF therapy in patients with RA*

Role: PI

R01 AR059648 Plenge (PI) 8/01/2010-6/30/2012

NIH-NIAMS

Deep Re-Sequencing of Rheumatoid Arthritis Risk Loci

*Goal: Next-generation sequencing of coding exons from 30 genes identified by GWAS*

Role: PI

U54 LM 008748 Kohane (PI) 9/15/10-9/14/14  
NIH National Center for Biomedical Computing  
*Create an informatics infrastructure to mine electronic medical records for discovery research purposes.*  
Role: PI on sub-contract

U54 HL 117798 FitzGerald (PI) 5/01/2012-4/30/2014  
NIGMS  
Personalization of therapeutic efficacy and risk  
*Goal: Conduct a 2-year pilot project linking clinical data from the EMR to discarded biospecimens.*  
Role: PI on sub-contract

Harvard Catalyst Child Health Plenge (PI) 5/01/2012-4/30/2013  
Harvard Medical School  
Novel autoantigen discovery with a synthetic human peptidome in juvenile idiopathic arthritis  
*Goal: Pilot project to discover autoantigens and correlate with clinical features in JIA.*  
Role: PI

Broad SPARC/Arthritis Foundation Plenge (PI) 9/01/2012-8/31/2013  
Broad Institute and the Arthritis Foundation  
Genomic analysis in the arthritis internet registry (AIR) cohort  
*Goal: Pilot project to perform GWAS and expression analysis in 300 AIR patients*  
Role: PI

**Recently Completed Research Support (selected)**

K08 AI55314 Plenge (PI) 5/01/04-1/31/09  
NIH-NIAID  
*The goal of this mentored training grant was to study the genetic basis of the immune response.*

U54 RR020278 Plenge (PI) 9/01/06-08/31/07  
National Center for Research Resources (NCRR)  
*The goal was to perform subsidized genotyping of a GWAS of rheumatoid arthritis risk.*

Gate's Foundation, #43307 Walker (PI) 9/01/07-09/30/08  
Gate's Foundation  
*The goal of this study was to conduct a GWAS to search for genetic predictors of HIV viral load*  
Role: co-investigator on the subcontract

2008A053376 Plenge (PI) 5/1/08-4/30/09  
Hearst Young Investigator Award;  
*The goal of this career award was to study the clinical and biological significance of RA risk alleles.*

U54 LM 008748 Kohane (PI) 8/01/07-7/31/10  
NIH National Center for Biomedical Computing  
*Create an informatics infrastructure to mine electronic medical records for discovery research purposes.*  
Role: PI on sub-contract

Research and Education Foundation Plenge (PI) 7/01/08-6/31/10  
American College of Rheumatology  
*Conduct a candidate gene and pilot GWAS of response to anti-TNF therapy in rheumatoid arthritis.*

R01 AR057108 Plenge (PI) 5/12/2009-4/30/2011  
NIH-NIAMS  
Meta-analysis of GWAS data to identify novel rheumatoid arthritis risk loci.  
*Goal: Perform a meta-analysis of GWAS data to identify novel rheumatoid arthritis risk loci*