SickleGen and Sickle Cell Genomics

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(12/09/11)

SickleGen PIs

Paola Sebastiani Clinton Baldwin	Boston University
Michael DeBaun	Washington Univ., Vanderbilt
James Casella	Johns Hopkins
Victor Gordeuk	Howard
Mark Gladwin	Univ. of Pittsburgh
Marilyn Telen	Duke
Greg Kato James Taylor	NHLBI
Carolyn Hoppe	Children's Hospital Oakland
Abdulrahman Alsultan	King Saud Univ., Riyadh
Amein Al-Ali	King Faisal Univ., Dammam

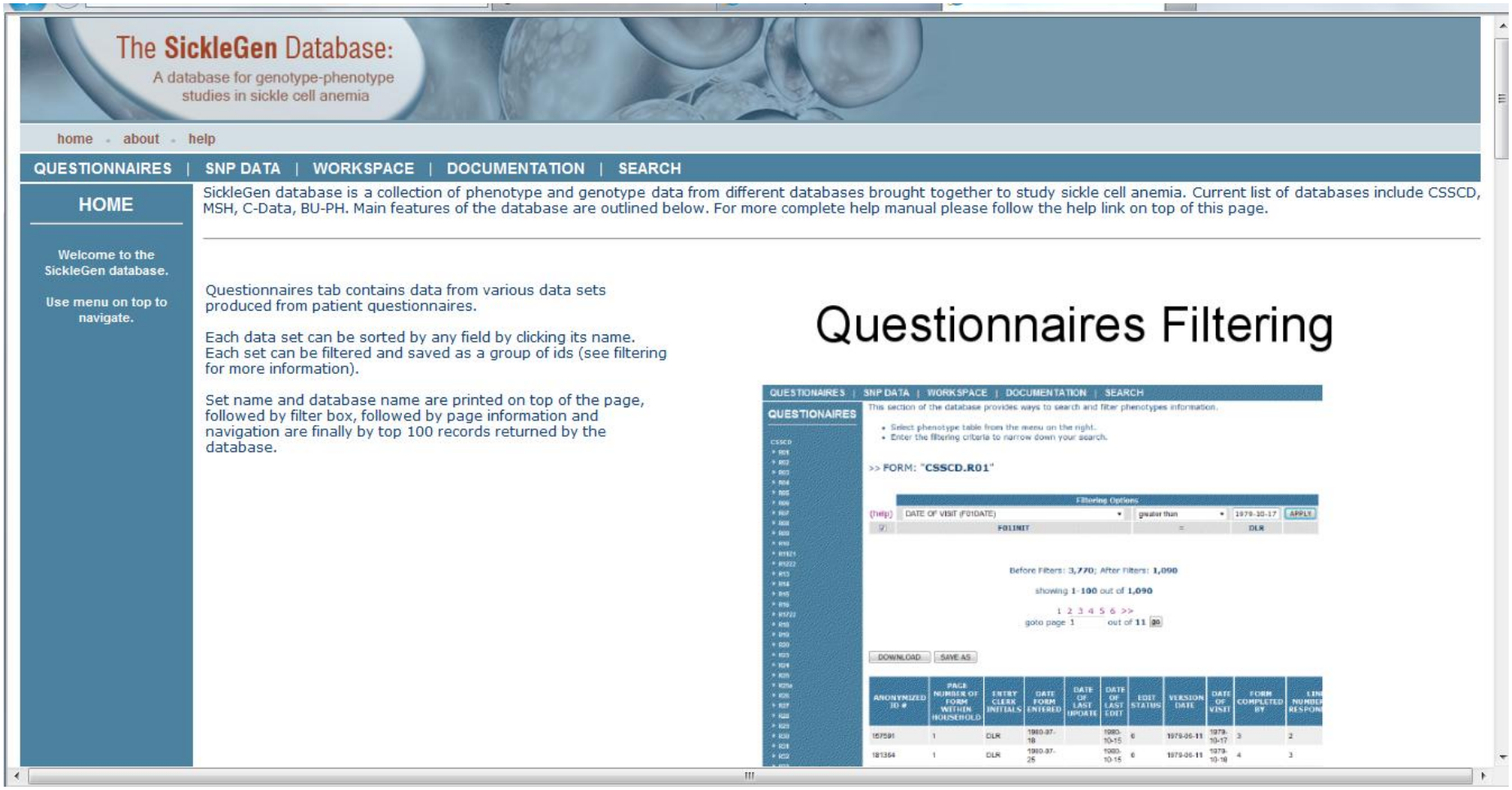
Sharing: Summary data on dbGaP, individual data shared among SickleGen and outside investigators, individual data on dbGap awaiting approvals

Cohorts Already Genotyped with Phenotypes and Biological Samples

Center/PI/Grant	Source/ Cases
BU/Steinberg/HL068970; HL78681	CSSCD/1500
BU/Steinberg/HL70735	MSH/280
BU/Klings/K23HL79003	BMC/200
Children's Hospital Oakland/Hoppe/U54 HL70583	CSCC C-data Gen-Phen project/600
Pittsburg/Gladwin/ HHSN 2680061784C	Walk-PHaSST/635
Duke/Telen/HL079915; HL68959	Outcome and Modifying Genes in Sickle Cell Disease/PH in SCD/500
Howard/Gordeuk/HL79921	PUSH/510
Vanderbilt/Hopkins/DeBaun, Casella/NINDS U01 NS042804	SITT trial/1130 collected (additional collections ongoing)
NIH/NHLBI/Taylor	NIH PH Study/530
King Faisal/Al-Ali/HL068970	HbF in Saudi Arabia/200

SickleGen Database

We created a database with free access to investigators who contributed genetic and phenotypic data



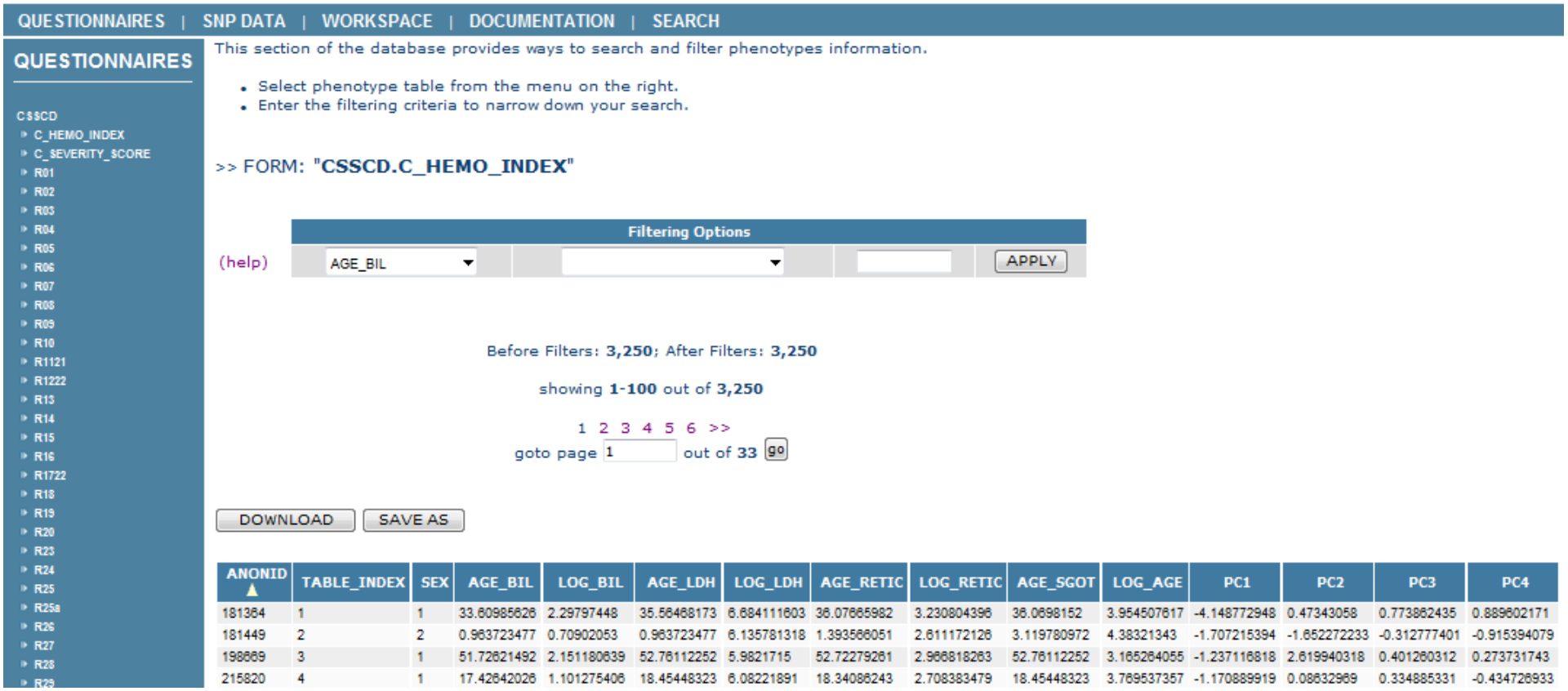
http://lobstah.bu.edu/gdd2/

SickleGen Database

Five studies included. The database includes all data from the 3 phases of the CSSCD study and derived variables

SickleGen Database

Site-Adjusted Variables and Hemolytic Index in CSSCD



QUESTIONNAIRES | SNP DATA | WORKSPACE | DOCUMENTATION | SEARCH

QUESTIONNAIRES

This section of the database provides ways to search and filter phenotypes information.

- Select phenotype table from the menu on the right.
- Enter the filtering criteria to narrow down your search.

CSSCD
- C_HEMO_INDEX
- C_SEVERITY_SCORE
- R01
- R02
- R03
- R04
- R05
- R06
- R07
- R08
- R09
- R10
- R1121
- R1222
- R13
- R14
- R15
- R16
- R1722
- R18
- R19
- R20
- R23
- R24
- R25
- R25a
- R26
- R27
- R28
- R29

>> FORM: "CSSCD.C_HEMO_INDEX"

Filtering Options

(help) AGE_BIL APPLY

Before Filters: 3,250; After Filters: 3,250

showing 1-100 out of 3,250

1 2 3 4 5 6 >>

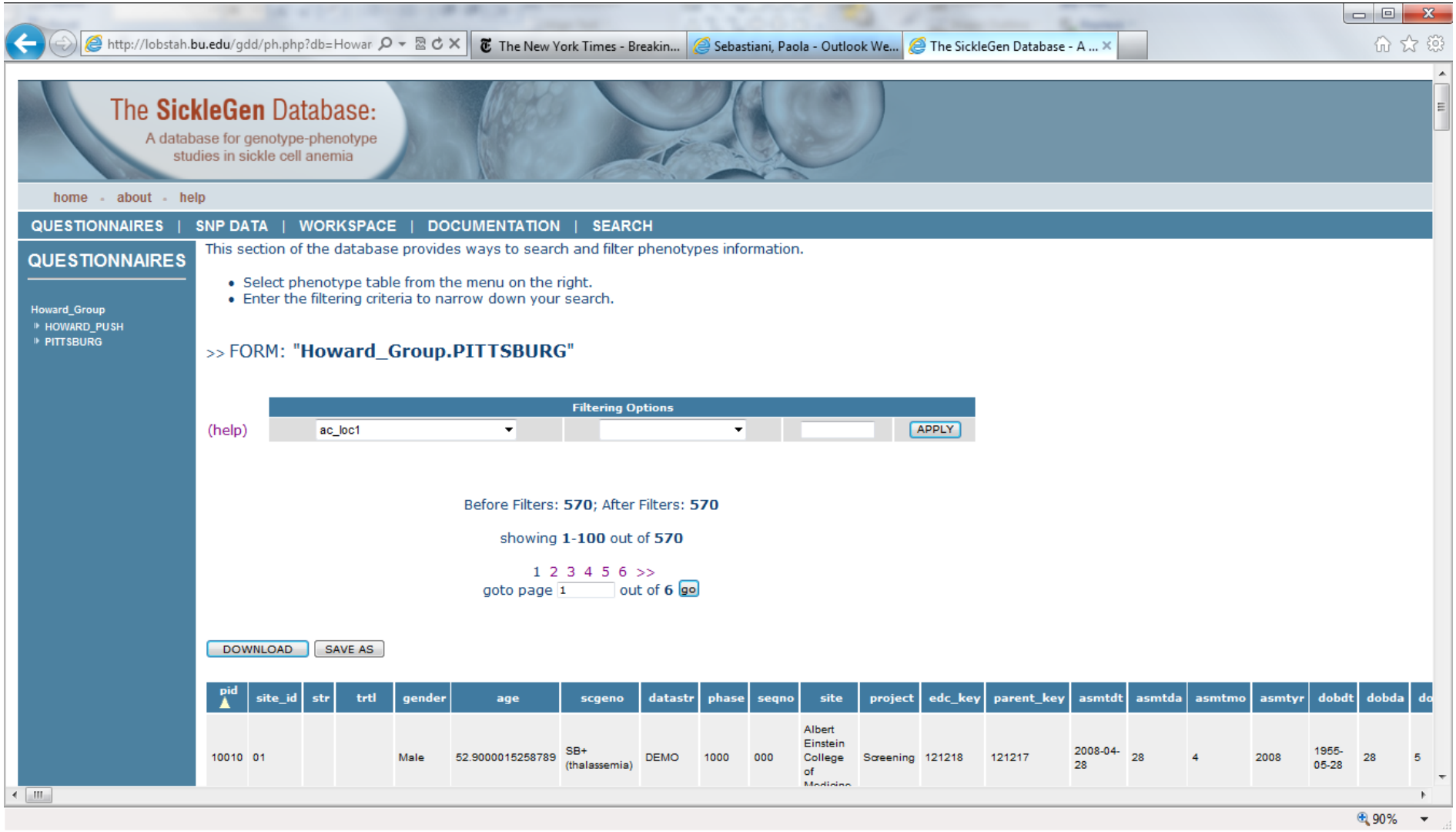
goto page 1 out of 33 go

DOWNLOAD SAVE AS

ANONID	TABLE_INDEX	SEX	AGE_BIL	LOG_BIL	AGE_LDH	LOG_LDH	AGE_RETIC	LOG_RETIC	AGE_SGOT	LOG_AGE	PC1	PC2	PC3	PC4
181364	1	1	33.60985626	2.29797448	35.56468173	6.684111603	36.07665982	3.230804396	36.0698152	3.954507617	-4.148772948	0.47343058	0.773862435	0.889602171
181449	2	2	0.963723477	0.70902053	0.963723477	6.135781318	1.393566051	2.611172126	3.119780972	4.38321343	-1.707215394	-1.652272233	-0.312777401	-0.915394079
198669	3	1	51.72621492	2.151180839	52.76112252	5.9821715	52.72279261	2.966818263	52.76112252	3.165284055	-1.237116818	2.619940318	0.401260312	0.273731743
215820	4	1	17.42642026	1.101275406	18.45448323	6.08221891	18.34086243	2.708383479	18.45448323	3.769537357	-1.170889919	0.08632969	0.334885331	-0.434726933

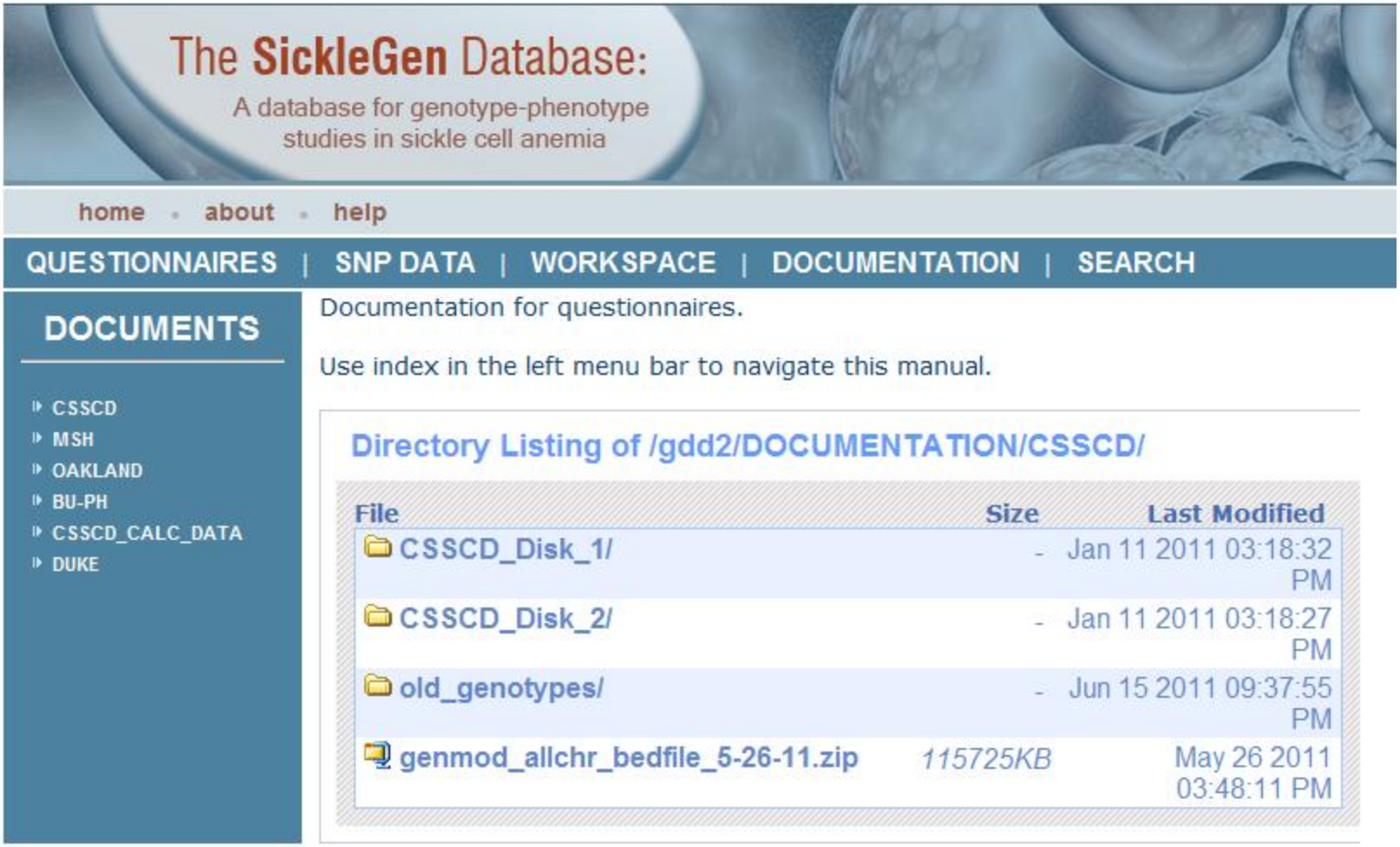
SickleGen Database

Phenotype Data

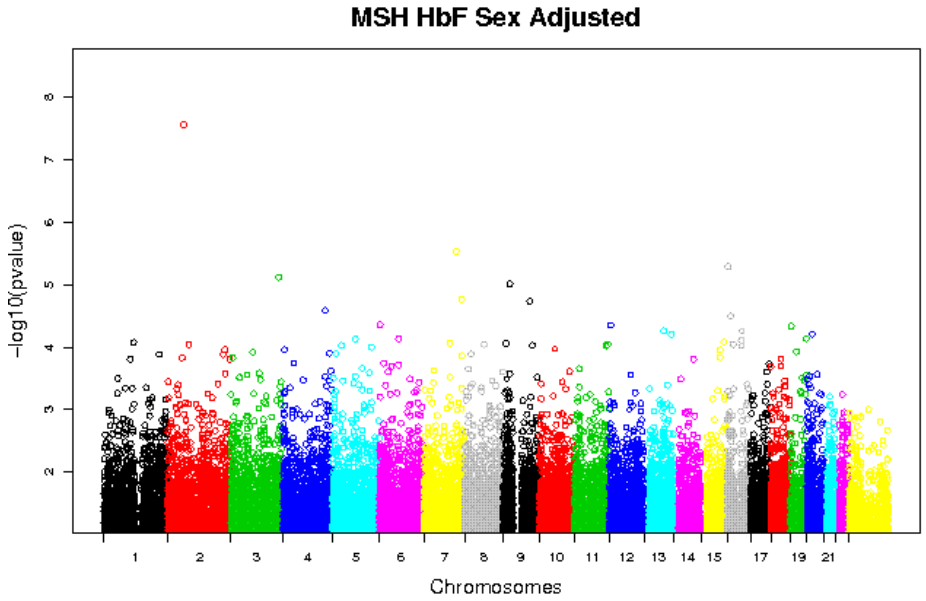


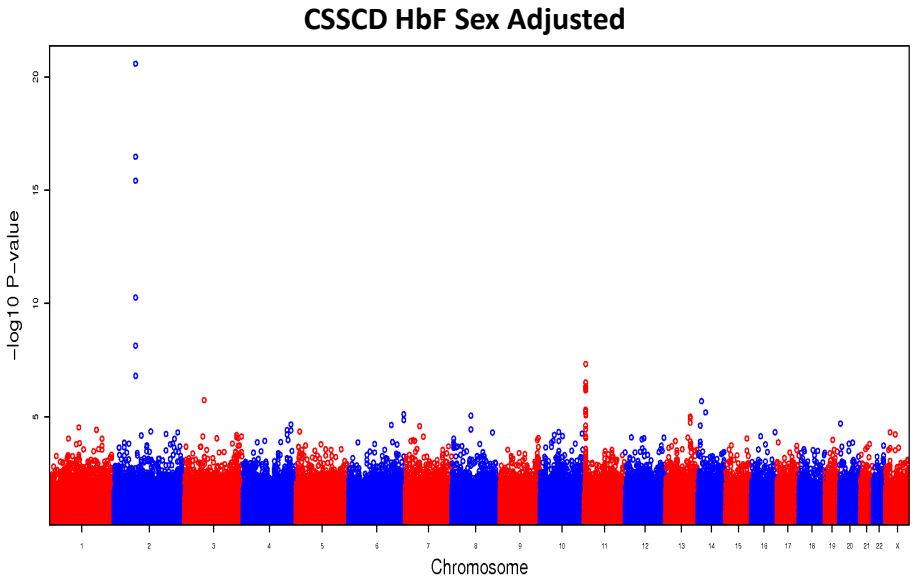
SickleGen Database

Genotype Data



SickleGen GWAS Studies (HbF)



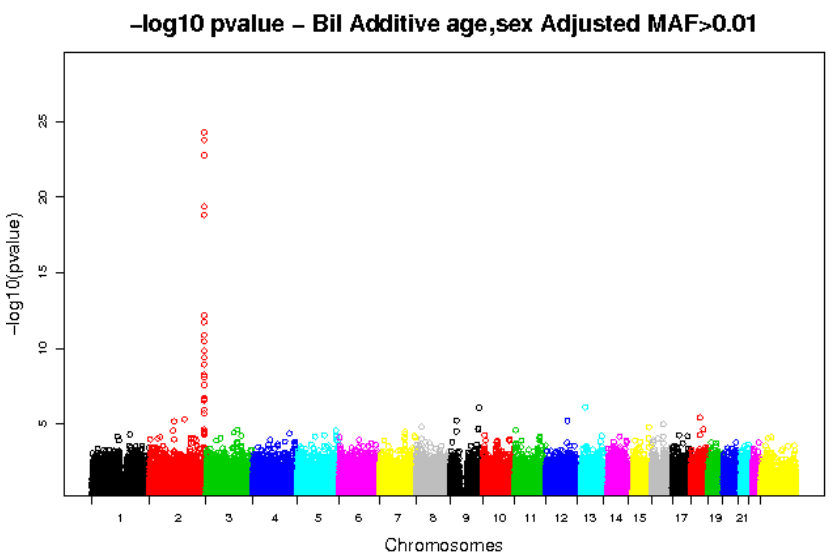


Sedgewick, A.E., Timofeev, N., Sebastiani, P., So, J.C.C., Ma, E.S.K., Chan, L.C., Fucharoen, G., Fucharoen, S., Barbosa, C.G., Vardarajan, B., Farrer, L.A., Baldwin, C.T., Steinberg, M.H., Chui, D.H.K. *BCL11A* is a major HbF quantitative trait locus in three different populations with β-hemoglobinopathies. Blood Cells Mol. and Dis. 41: 255, 2008.

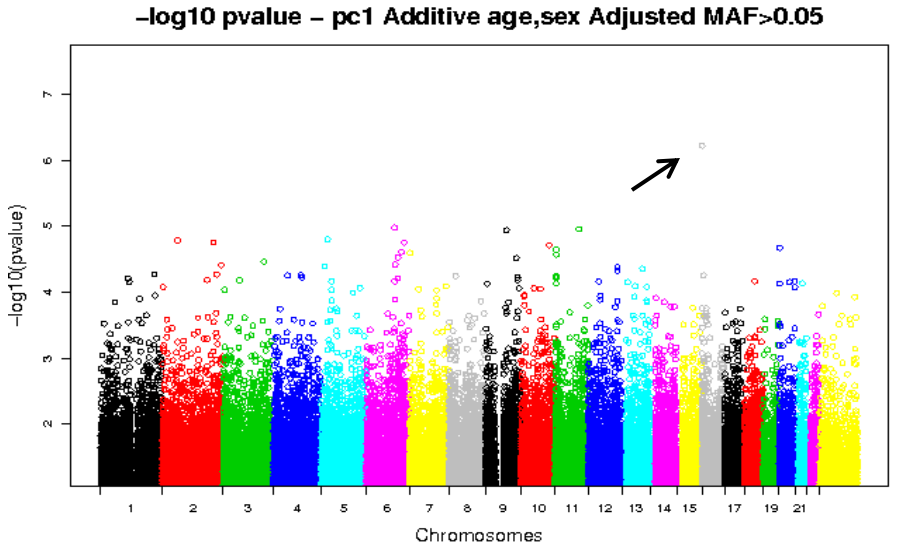
Solovieff, N., Milton, J.N., Hartley, S.W., Sherva, R., Sebastiani, P., Dworkis, D.A., Klings, E.S., Farrer, L.A., Garrett, M.E., Ashley-Koch, A., Telen, M.J., Fucharoen, S., Ha, S.Y., Li, C.K., Chui, D.H.K., Baldwin, C.T., Steinberg, M.H. Fetal hemoglobin in sickle cell anemia: Genome-wide association studies suggest a regulatory region in the 5' olfactory receptor gene cluster. Blood 115: 1815, 2010.

SickleGen GWAS Studies (others)

Bilirubin: *UGT1A1*



Hemolysis: *NPRL3*



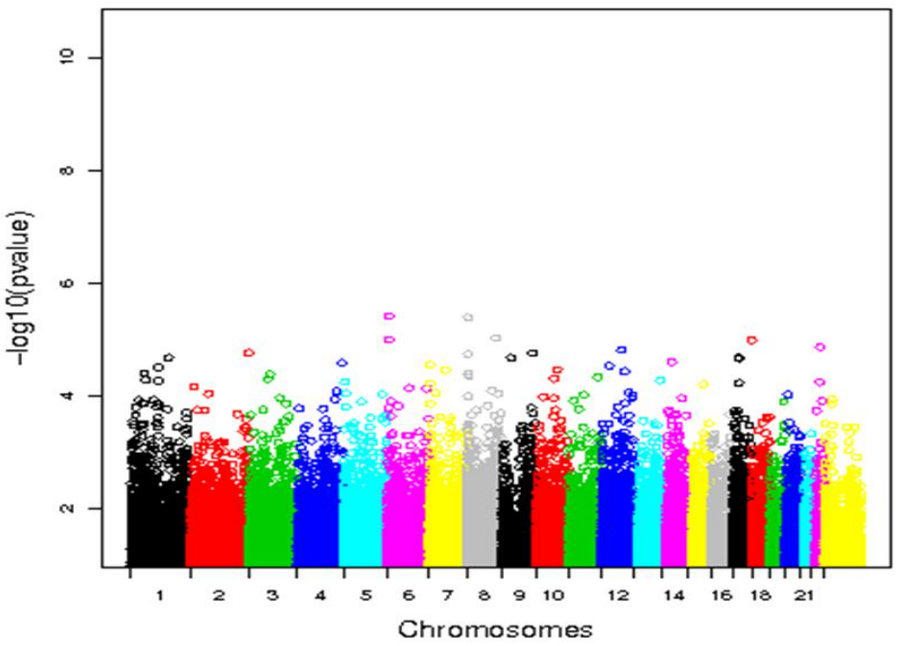
Milton, J.N., Sebastiani, P., Solovieff, N., Hartley, S.W., Bhatnagar, P., Arking, D.E., Dworkis, D.A., Casella, J.F., Barron-Casella, E., Bean, C.J., Hooper, W.C., DeBaun, M.R., Garrett, M.E., Soldano, K., Telen, M.J., Ashley-Koch, A., Gladwin, M.T., Baldwin, C.T., Steinberg M.H., Klings, E.S. A genome-wide association study of total bilirubin and cholelithiasis risk in sickle cell anemia 2011 (submitted).

Milton, J.N., Sebastiani, P., Zhang, Y., Nouraie, M., Lee, J. Baldwin, C.T., Zhao, X., Xiong, Z., Zeng, Q., Kato, G.J., Goldsmith, J.C., Taylor, J.G., Gordeuk, V.R., Machado, R.F., Steinberg, M.H., Gladwin, M.T. Clinical and genetic variability of red blood cell hemolysis in sickle cell disease. Blood ASH 2011.

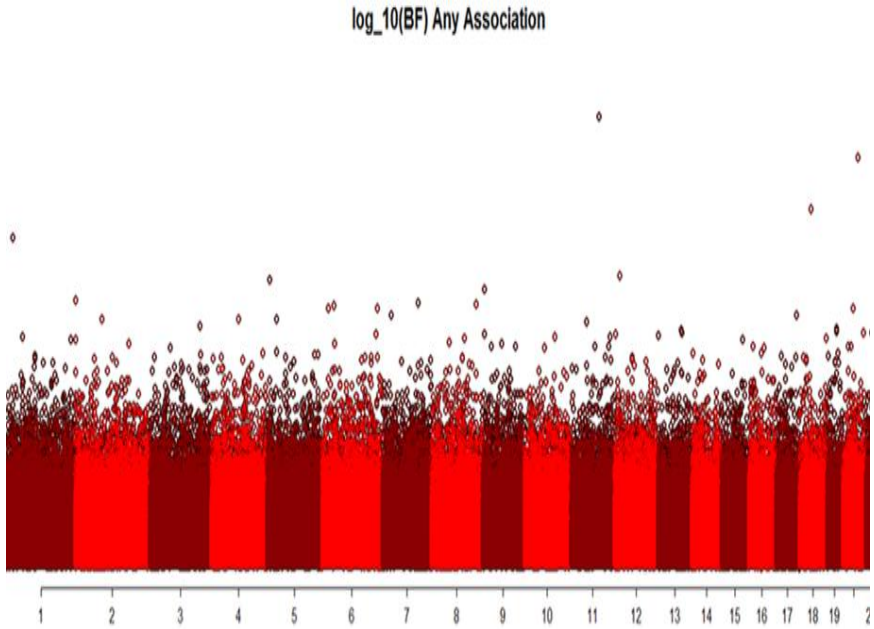
Solovieff, N., Hartley, S.W., Baldwin, C.T., Klings, E.S., Gladwin, M.T., Taylor, J.G.IV, Kato, G.J., Farrer, L.A., Steinberg, M.H., Sebastiani P. Ancestry of African Americans with sickle cell disease. 2011 Blood Cells Mol and Dis 47: 41, 2011.

SickleGen GWAS Studies (others)

TRV: *CSMD1*



Severity score: *KCNK6, TNKS*



Bae, H., Baldwin, C.T., Gladwin, M.T., Ashley-Koch, A.E., Garrett, M., Soldano, K., G. Taylor, J.G., Kato, G.J., Telen, M.T., Sebastiani, P., Steinberg, M.H., Klings, E.S. An elevated tricuspid regurgitant jet velocity in sickle cell disease is associated with polymorphisms in genes impacting innate immunity . Blood ASH 2011.

Sebastiani, P., Timofeev, N., Hartley, S.W., Milton, J.N., Riva, A., Dworkis, D.A., Klings, E.S., Garrett, M.E., Telen, M.J., Ashley-Koch, A., Baldwin, C.T., Steinberg, M.H. Genetic modifiers of the severity of sickle cell anemia identified through a genome-wide association study. Am. J. Hematol 85: 29, 2010.

SickleGen: in progress and in the future

Other subphenotypes for GWAS

- Heritability of traits
- Hematologic parameters
- Pain
- Acute chest syndrome
- Blood pressure
- Nephropathy
- HbF response to HU
- Meta-analysis of HbF
- HbF in Saudi Arabs

Next-gen sequencing and RNA-seq

- Saudi Arabs
- "Discordant" sib-pairs
- QTL-specific iPS cells