Services we provide

Statistical Genetics Analysis Division
StaGen Co., Ltd.

Three key words for SGA in StaGen

Study design

case group

disease

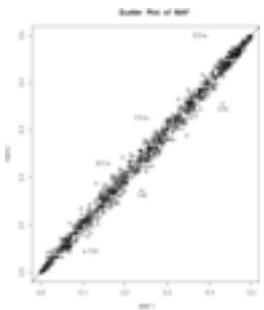
control group

non-disease

How large should the size be to achieve 80% power in case-control studies for a SNP with the odds ratio of 3?

Appropriate study design to avoid incorrect conclusions

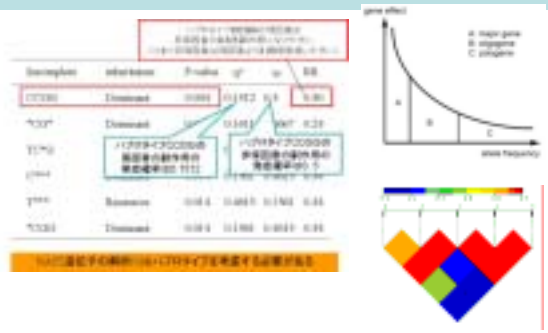
Quality control of genotype data



It is inevitable to remove genotype data which are incorrect or not in accord with the laws of inheritance. Multiple comparison problem in genome-wide SNP analysis should also be considered.

Unreliable information is eliminated and incorrect results are avoided.

Analysis based on laws of inheritance



For obtaining reliable conclusions, genome-wide association study (gwa) and haplotype association study should be based on the laws of inheritance. Multiple comparison problem in gwa is critical.

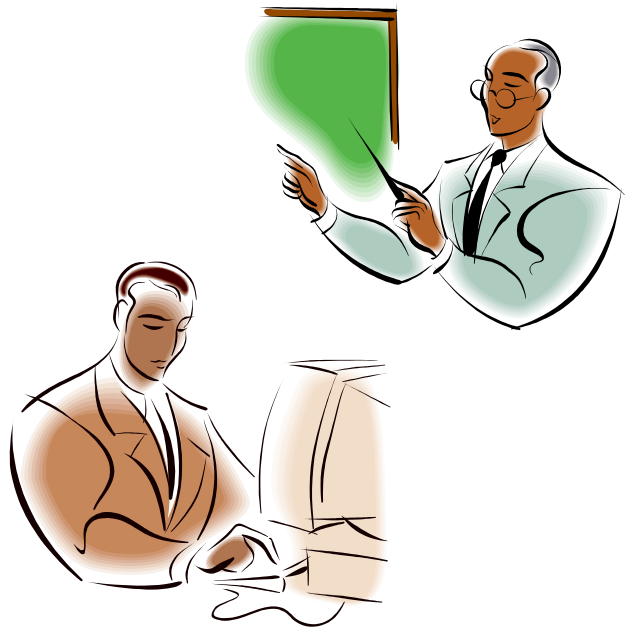
Analysis based on the laws of inheritance to obtain the results with high reproducibility.

“Sophisticated” Statistical Genetics Analysis＝SGA

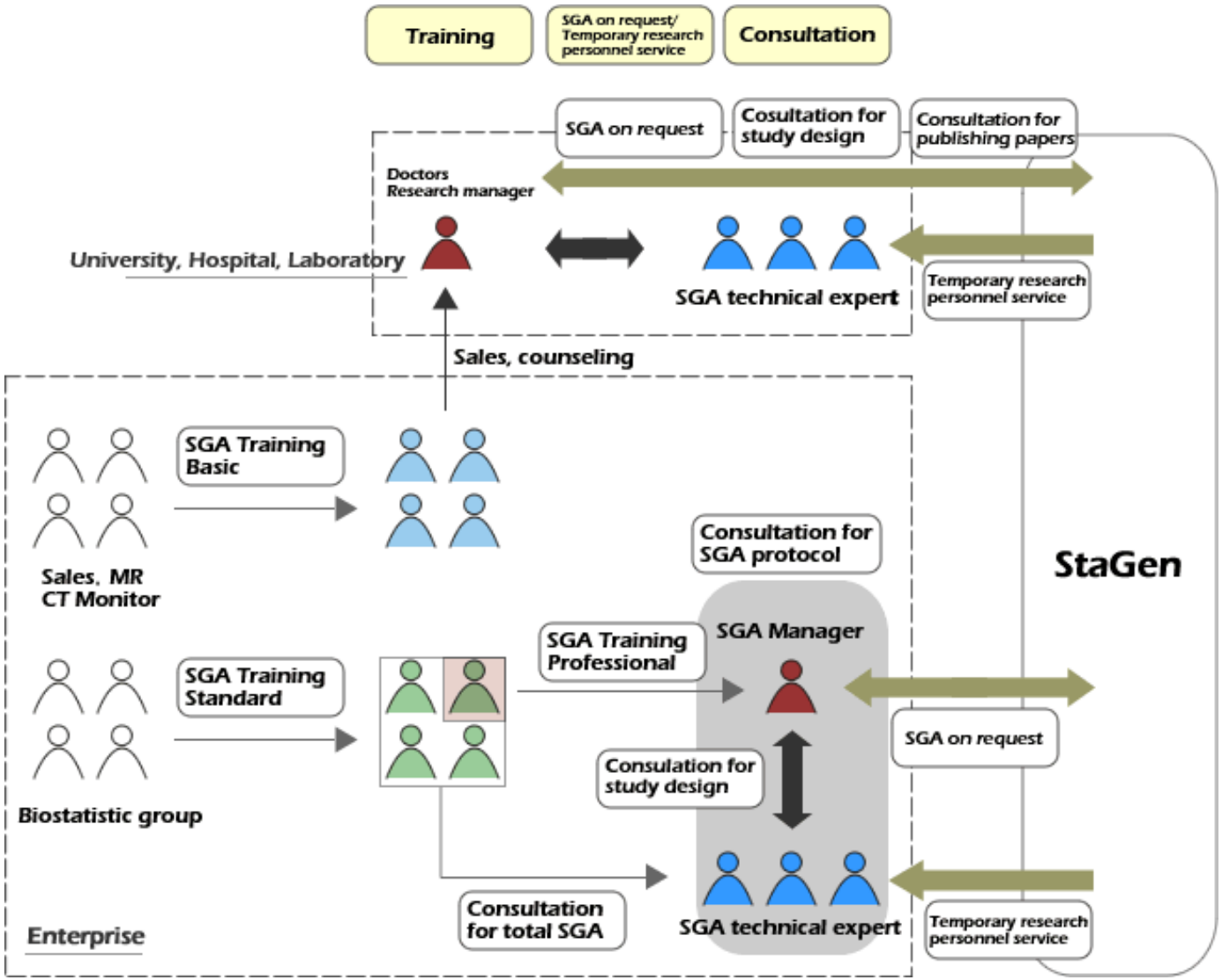
Services provided by SGA division

We provide various services in SGA for our customers.

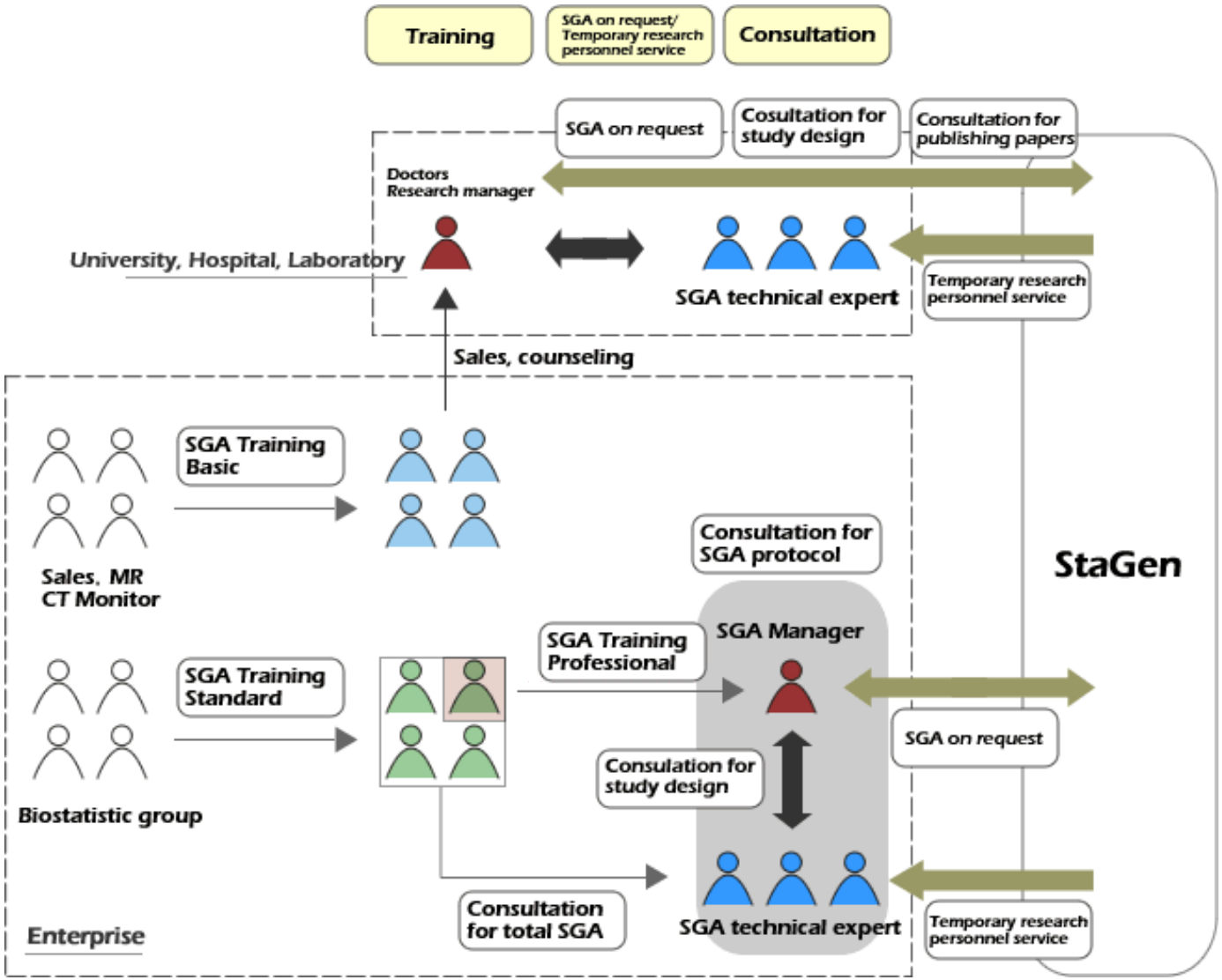
- Training in SGA
- SGA on request
- Temporary research personnel service
- Consultation in SGA
- System development



Summary of Our Services



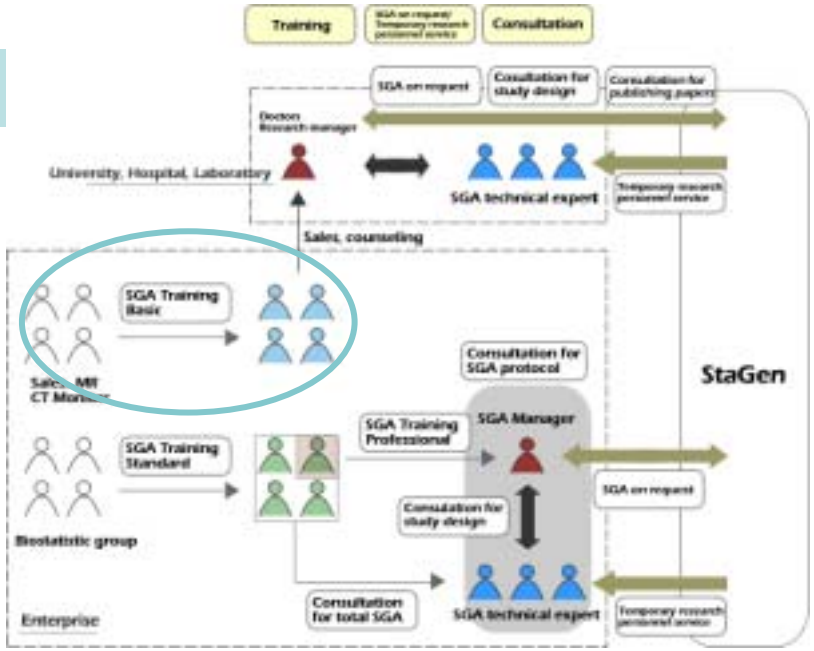
SGA Training service

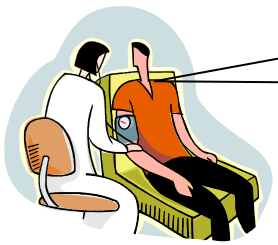


SGA training: Basic course

Fundamental knowledge about PGx

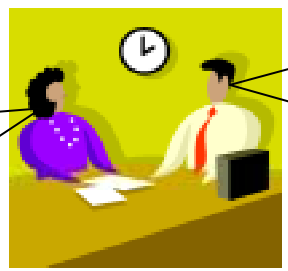
- What is the purpose of PGx?
- How can we extract knowledge from PGx?
- How can the results from PGx be applied?





Genome study may provide you with medicine with higher quality.

How has the evidence for the association between the adverse events and a genetic polymorphism been obtained?



This result was obtained by a GWA study. There is a report that the patients with genotype A/A at locus y in gene *x* have 2.8 times more chance to suffer from the adverse events by the drug.

Knowledge about PGx is necessary for various professionals such as drug-developers, medical doctors, nurses, medical representatives (MR), genetic counselors, and pharmacists.

SGA training: Standard course

Acquisition of higher level knowledge about PGx

- Relationship between biological data and laws of inheritance
- Understanding of the mathematical aspects of SGA
- Exercise using SGA tools

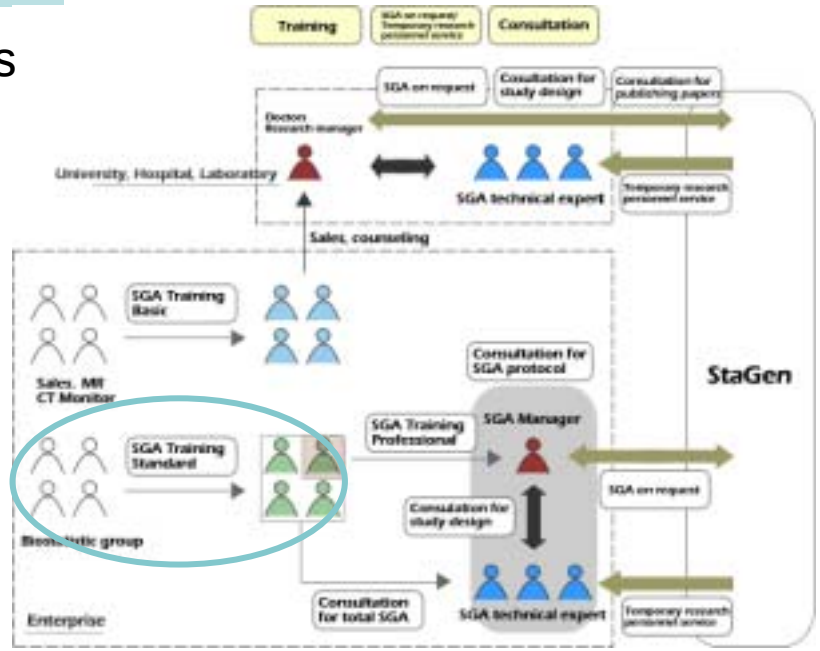
"Introduction of statistical genetics"

by Naoyuki Kamatani

+

Concise explanation

by StaGen

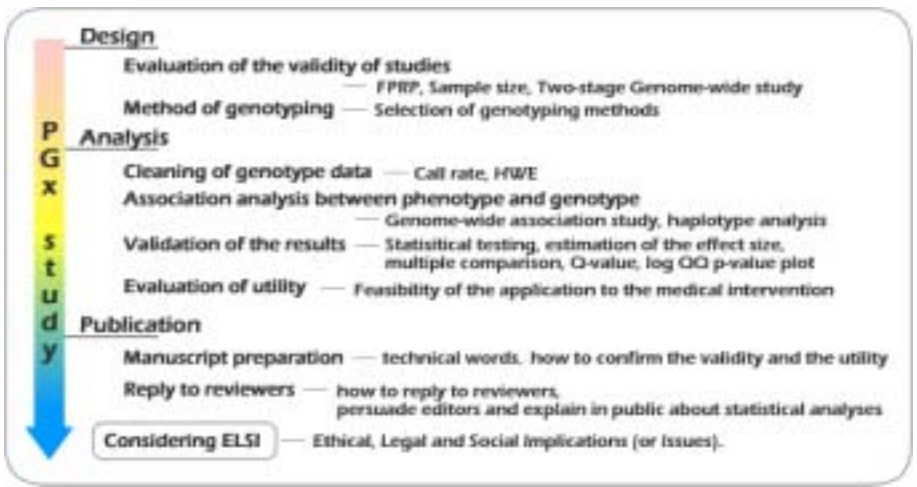


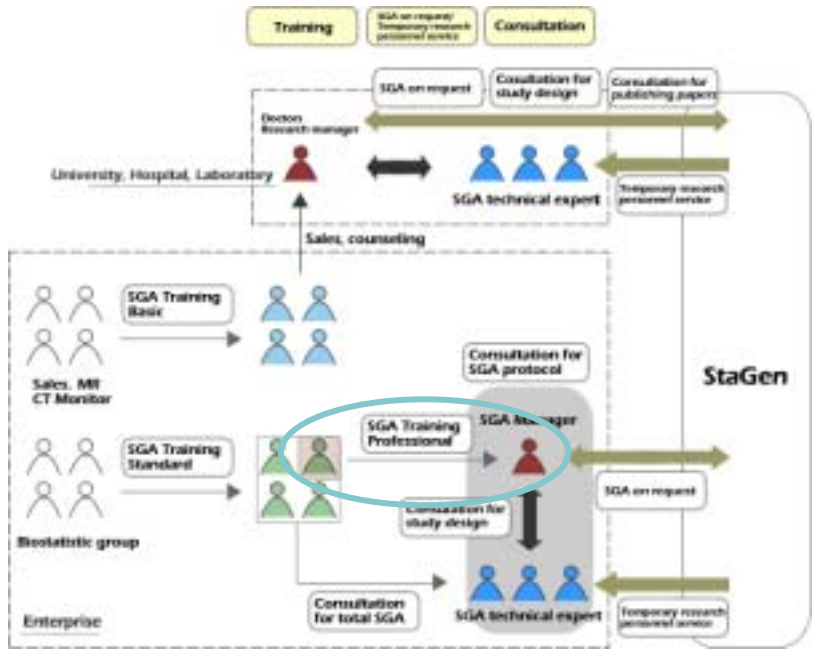
Education of knowledge and techniques in statistical genetics for SGA managers and SGA technicians

SGA training: Professional course

Training course for SGA managers

- Optimal designing of PGx studies given various factors
- Training for practical PGx studies using simulation and real samples





Training for SGA managers as supervisors of PGx studies

SGA education
3 training courses

	SGA training		
	Basic	**Standard**	**Professional**
Goal	Acquisition of fundamental knowledge about SGA	Acquisition of statistical theories and procedures in SGA	Acquisition of more specialized knowledge of SGA
Target	MR, clinical trial monitors and other employees of drug companies and research institutions (Prior knowledge of statistitics or genetics not necessary)	Researchers and employees who need SGA in business and researches	Researchers and employees who have learned in SGA training standard course or those with equivalent abilities
Scale	Large	15～25 people/class	A few
Style	Intensive course	Intensive course	Seminar
Term	3 hours	25 hours	Flexible

Curriculum adjusted to customers' needs

SGA Training Standard course

- ☑ Differences between SGA and general statistics
- ☐ Chromosome and genetic information
- ☐ Meiosis, Meitosis and inheritance
- ☑ Laws of inheritance
- ☑ Polymorphisms and variations
- ☑ Haplotype and LD
- ☐ Linkage analysis
- ☑ Association study
- ☑ Study design and Qualitiy of data
- ☑ Pharmacogenetics
- ☐ Data Science

Total : 25 hours

→

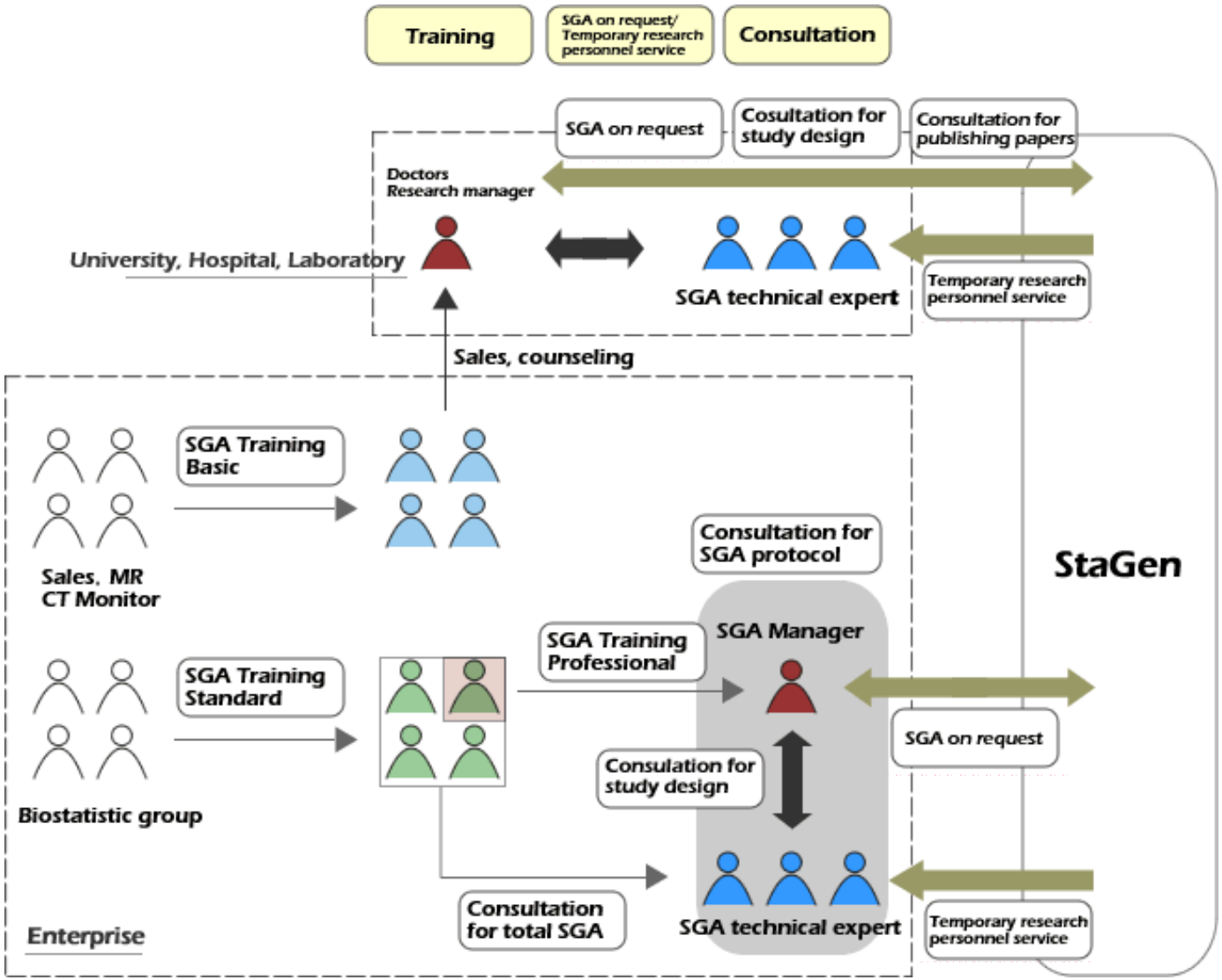
SGA Training Standard course

- ☐ Differences between SGA and general statistics
- ☐ Laws of inheritance
- ☐ Polymorphisms and variations
- ☐ Haplotype and LD
- ☐ Association study
- ☐ Study design and Qualitiy of data
- ☐ Pharmacogenetics

Total : 15 hours

We provide the optimized curriculum considering the backgrounds of our customers.

SGA on request and temporary research personnel service



SGA on request and temporary research personnel service

Analysis of your data by SGA specialists in either your laboratory or our laboratory

- High quality SGA based on our protocol
- Analysis based on original algorithms developed by Naoyuki Kamatani, M.D., Ph.D, Tokyo Women's Medical University

ERS (in Japan)

Qualification of temporary personnel service (in Japan)

PGx study system under the leadership of SGA manager

Examples of SGA

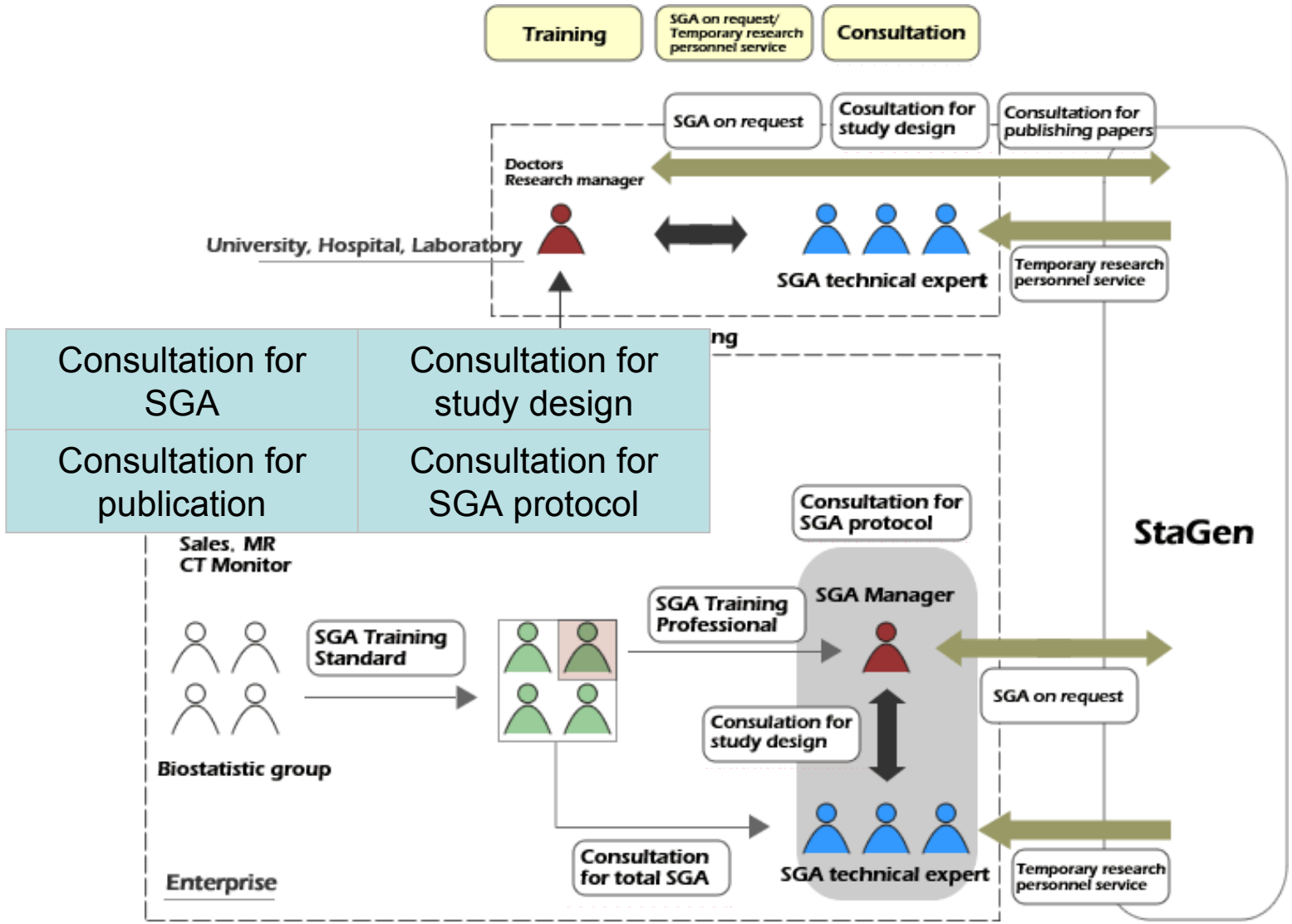
Category	Contents	
Establishment of framework	Construction of the data format	
	Construction of the framework for SGA	
Preparation for research	Designing of research study	
	Evaluation of previous researches	
Data cleaning	Removal of inappropriate data	Outoff threshold for call rate
		Evaluation by replication test
		Evaluation by MAF
		Comparison of the data between different conditions
		Estimation of typing error rate
		Use of the data for sex chromosomes based on biological laws
	Fitness to the laws of inheritance	Test of goodness of fit to HWE
Association study	Genome-wide SNP research	Statistical test
		Evaluation by log QQ p-value plot or FDR (Q-Value)
	Diplotype configurations (haplotype) association study	Determination of LD block
		Test of association based on diplotype configurations study
		Inference of diploype configurations
		Haplotype inference and test of association based on haplotypes
	Pedigree data analysis; linkage analysis	Parametric linkage analysis
		Nonparametric linkage analysis
		TDT (Transmission Disequilibrium Test)
Others	Examination of population structure	
	Evaluation by meta analysis	

Original algorithms developed under the supervision of Naoyuki Kamatani, M.D., Ph.D, Tokyo Women's Medical University

- Pooled DNA
  - Ldpooled (Ito et al. Am J Hum Genet 72: 384-398, 2003)
    - Inference of haplotype frequencies using pooled DNA data
- Inference of haplotype and diplotype configurations
  - AssignHaplo (Kamatani et al. Am J Hum Genet 75: 190-203, 2004)
    - Uncommon SNPs in LD block are assigned to major haplotype
  - Ldsupport (Kitamura et al. Ann Hum Genet 66: 183-193, 2002)
    - Inference of haplotype frequencies in the population and individual diplotype configurations by maximum likelihood method
- Cluster analysis
  - Popstruct (Nakamura et al. J Hum Genet 50: 53-61, 2005)
    - Test of structuring of the population in case-control study, cohort study or clinical trial
- Phenotype association study
  - Multilocustest (Fujii et al. Takeda Symposium)
    - Test of multiple SNP loci using data from cohort, clinical trial and case-control
  - Penhaplo (Ito et al. Genetics 168: 2339-2348, 2004)
    - Test of association between qualitative phenotype and diplotype configurations and inference of penetrances using the data from cohort, clinical trial and case-control
    - (Furihata et al. Genetics 174: 1505-1516, 2006)

      Test of association between haplotypes and phenotypes in case-control studies: examination of validity of the application of an algorithm for samples from cohort or clinical trials to case-control samples using simulated and real data.
  - QTLhaplo (Shibata et al. Genetics 168: 525-539, 2004)
    - Test of association between quantitative phenotype and diplotype configurations and inference of penetrances using the data from cohort, clinical trial and case-control
  - QTLmarc (Kamitsuji et al. J Hum Genet 51: 314-325, 2006)
    - Inference of haplotypes associated with several quantitative phenotypes

Consultation services



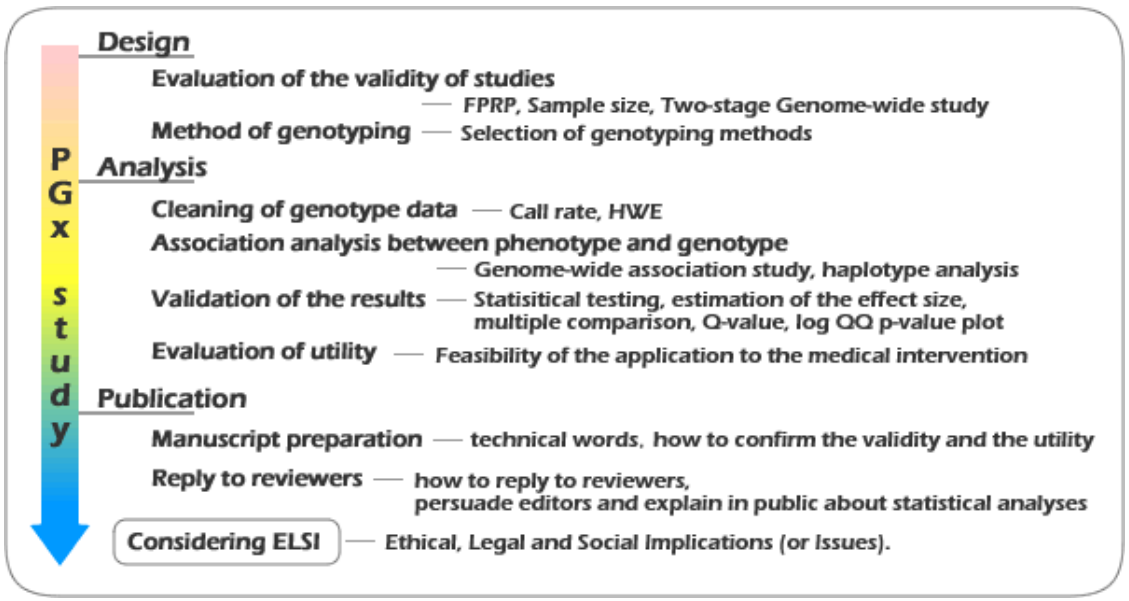
Consultation for total SGA

Improvement of SGA knowledge and techniques by SGA consultant

- Solution by SGA consultant
  - Improvement of the ability of SGA manager
  - Accumulation of SGA knowledge・technique
    - Training of SGA technician

Algorithms of PENHAPLO, QTLHAPLO are available

Consultation for PGx study



Consultation for study design

Study designs for candidate gene-based and genome-wide association studies

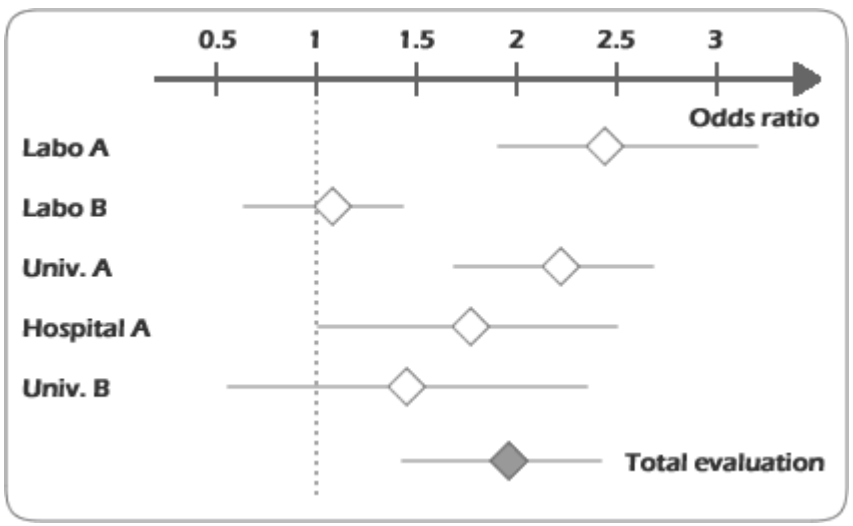
Study designs for candidate gene-based association studies

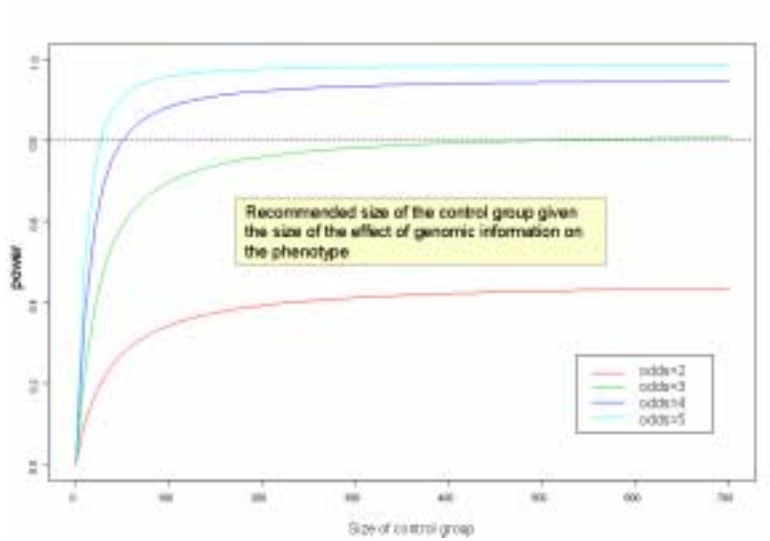
Previous researches are evaluated and

studies are designed based on the evaluation

- Evaluation using FPRP or power
- Integrated evaluation of previous researches using meta analysis
- Simulations for sample size and power under various conditions

There are some reports that a mutation in a gene is associated with adverse events of a medicine. Although we plan to conduct a case-control study based on the evaluation of the previous researches, it is difficult to collect more than 30 people as the case group. How many control people are needed for the significant result?

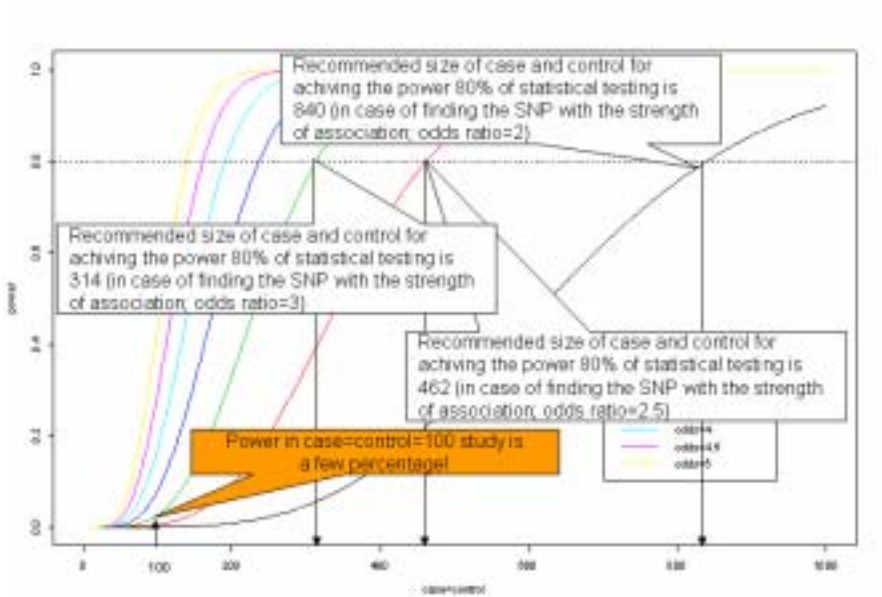


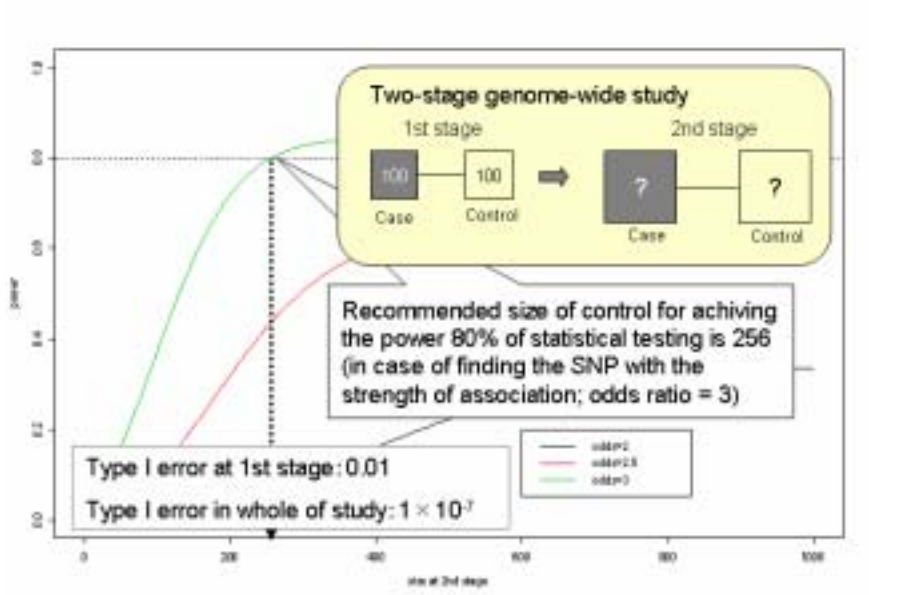


Consultation for study design

Study design of genome-wide association study

We want to find a candidate gene associated with a disease by genome-wide association study. We want to optimize the design of the study.





proposal	power	method	Typing sample size		Typing number		cost
			stage 1	stage 2	stage 1	stage2	
request	3%	1-stage screening	100*2=200	-	500K	-	\30,000,000
proposal 1	80%	1-stage screening	314*2=628	-	500K	-	\94,200,000
proposal 2	50%	1-stage screening	236*2=472	-	500K	-	\70,800,000
proposal 3	80%	2-stage screening	100*2=200	256*2=512	500K	500K*0.01=5K	\35,120,000

＊ GeneChip 500K：150000yen/sample
＊ Individual typing：2yen/SNP

・Chip：500K DNAchip
・Carrier frequency of risk allele in control group：0.2
・Significance level：0.05.
・Multiple comparison：Bonferroni correction

Other consultations

Consultation for publication

- Statistical consultation for genome research in manuscript preparation
- Responses to reviewers about the statistical analysis, and explanation of the results in public

Consultation for SGA protocol

- Preparation of SGA protocol for obtaining reliable results
- SGA Training based on individual protocol is supplied.

We supply consultants who are experienced and familiarized in statistical genetics

- Specialist of statistics, medical science and computer infomatics.
- We are trained in statistical genetics under Prof. Naoyuki Kamatani, Tokyo Women's Medical University
- SGA experts in StaGen have many experiences in the analysis in Tokyo Women's Medical University, Japan Biological Informatics Consortium, National Cancer Center, and so on.

System development services

Development of computer system for SGA

- Construction and maintenance of computer system for SGA
  - Installation of original algorithms; PENHAPLO, QTLHAPLO
  - Suggestion and installation of other tools for SGA; statistical analysis language R etc…

We provide analytical tools for statistical genetics

Tool for study design

- Simulation tool to find optimal sample size and power
  - available under various conditions
- We also provide tools for training in study designing
  - theoretical background of study design
  - how to use this tool

Tool for association study

- Tool for implementing the genome-wide association study based on statistical genetics
  - Quantitative or qualitative phenotype is available.
  - Permutation test to evaluate the significance by generating the distribution of p-values is available.

Other business

Training Staff

- Kobe University・Translational Research Informatics Center
  - Training Unit; Clinical Genome Informatics (CGI)
- Tokyo Medical and Dental University
  - Training Program; Bio-Omics informatics

Media

- Nikkei Business Publications, Inc. monthly PDF magazine “BTJ journal” (in Japanese)
  - 「Welcome to statistical genetics!」 serialized from March

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