An Integrated Analysis Tool for Analyzing Hybridization Intensities and Genotypes Using New-Generation Population-Optimized Human Arrays

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A number of GWAS for tropical medicine and global health using SNP arrays were carried out

For AIDS

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Multistage Genomewide Association Study Identifies a Locus at 1q41 Associated with Rate of HIV-1 Disease Progression to Clinical AIDS

Joshua T. Herbeck[1], Geoffrey S. Gottlieb[2], Cheryl A. Winkler[3], George W. Nelson[3], Ping An[3], Brandon S. Maust[1], Kim G. Wong[1], Jennifer L. Troyer[3], James J. Goedert[5], Bailey D. Kessing[3], Roger Detels[8], Steven M. Wolinsky[10], Jeremy Martinson[11], Susan Buchbinder[9], Gregory D. Kirk[6], Lisa P. Jacobson[6], Joseph B. Margolick[7], Richard A. Kaslow[12], Stephen J. O'Brien[4], and James I. Mullins[1,2]

For Malaria

LETTER

doi:10.1038/nature11334

Genome-wide association study indicates two novel resistance loci for severe malaria

Christian Timmann[1,2], Thorsten Thye[1,2], Maren Vens[2], Jennifer Evans[1,3], Jürgen May[4], Christa Ehmen[1], Jürgen Sievertsen[1], Birgit Kings Andr

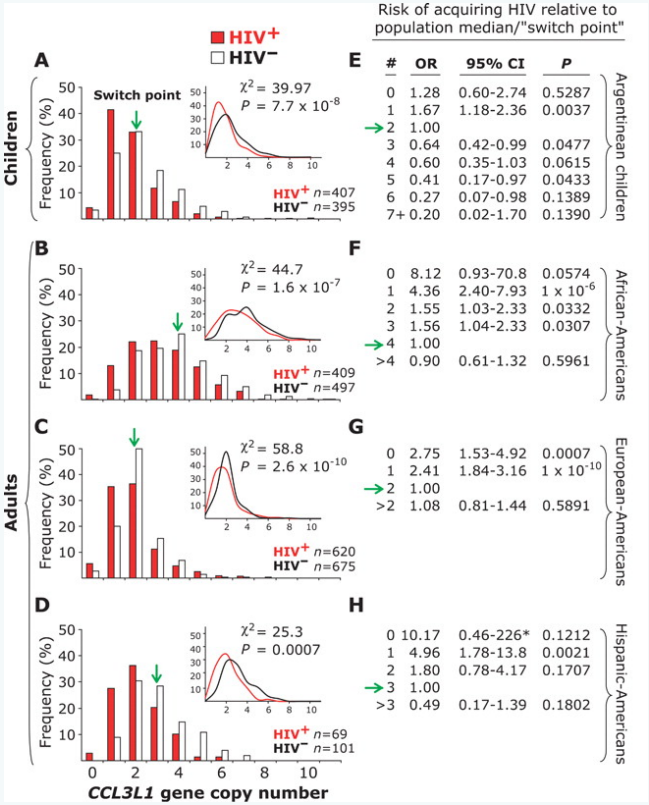
nature genetics

Genome-wide and fine-resolution association analysis of malaria in West Africa

Muminatou Jallow[1,34], Yik Ying Teo[2,3,34], Kerrin S Small[2,3,34], Kirk A Rockett[2,3], Panos Deloukas[3], Taane G Clark[2,3], Katja Kivinen[3], Kalifa A Bojang[1], David J Conway[1], Margaret Pinder[1], Giorgio Sirugo[1], Fatou Sisay-Joof[1], Stanley Usen[1], Sarah Auburn[2,3], Suzannah J Bumpstead[3], Susana Campino[2,3], Alison Coffey[3], Andrew Dunham[3], Andrew E Fry[2], Angela Green[2], Rhian Gwilliam[3], Sarah E Hunt[3], Michael Inouye[3], Anna E Jeffreys[2], Alieu Mendy[2], Aarno Palotie[3], Simon Potter[3], Jiannis Ragoussis[2], Jane Rogers[3], Kate Rowlands[2], Elilan Somaskantharajah[3], Pamela Whittaker[3], Claire Widden[3], Peter Donnelly[2,4], Bryan Howie[4], Jonathan Marchini[2,4], Andrew Morris[2], Miguel SanJoaquin[2,5], Eric Akum Achidi[6], Tsiri Agbenyega[7], Angela Allen[8,9], Olukemi Amodu[10], Patrick Corran[11], Abdoulaye Djimde[12], Amagana Dolo[12], Ogobara K Doumbo[12], Chris Drakeley[13,14], Sarah Dunstan[15], Jennifer Evans[7,16], Jeremy Farrar[15], Deepika Fernando[17], Tran Tinh Hien[15], Rolf D Horstmann[16], Muntaser Ibrahim[18], Nadira Karunaweera[17], Gilbert Kokwaro[19], Kwadwo A Koram[20], Martha Lemnge[21], Julie Makani[22], Kevin Marsh[19], Pascal Michon[8], David Modiano[23], Malcolm E Molyneux[5], Ivo Mueller[8], Michael Parker[24], Norbert Peshu[19], Christopher V Plowe[25,26], Odile Puijalon[27], John Reeder[8], Hugh Reyburn[13,14], Eleanor M Riley[13,14], Anavaj Sakuntabhai[27], Pratap Singhasivanon[28], Sodiomon Sirima[29], Adama Tall[30], Terrie E Taylor[25,31], Mahamadou Thera[12], Marita Troye-Blomberg[32], Thomas N Williams[19], Michael Wilson[20] & Dominic P Kwiatkowski[2,3], Wellcome Trust Case Control Consortium[33] & Malaria Genomic Epidemiology Network[33]

A number of studies showed CNVs are highly relevant to tropical diseases and global health

Enrique Gonzalez et al. Science 2005



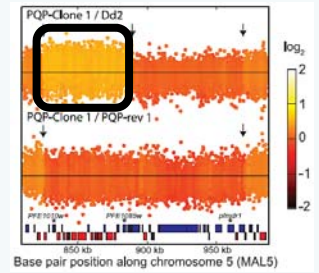
	#	OR	95% CI	P
A	0	1.28	0.60-2.74	0.5287
	1	1.67	1.18-2.36	0.0037
	→2	1.00		
	3	0.64	0.42-0.99	0.0477
	4	0.60	0.35-1.03	0.0615
	5	0.41	0.17-0.97	0.0433
	6	0.27	0.07-0.98	0.1389
	7+	0.20	0.02-1.70	0.1390
B	0	8.12	0.93-70.8	0.0574
	1	4.36	2.40-7.93	1 x 10⁻⁶
	2	1.55	1.03-2.33	0.0332
	3	1.56	1.04-2.33	0.0307
	→4	1.00		
	>4	0.90	0.61-1.32	0.5961
C	0	2.75	1.53-4.92	0.0007
	1	2.41	1.84-3.16	1 x 10⁻¹⁰
	→2	1.00		
	>2	1.08	0.81-1.44	0.5891
D	0	10.17	0.46-226*	0.1212
	1	4.96	1.78-13.8	0.0021
	2	1.80	0.78-4.17	0.1707
	→3	1.00		
	>3	0.49	0.17-1.39	0.1802

The **amplification** of the CCL3L1 **gene** was found to **reduce** the **risk** of HIV **progression**

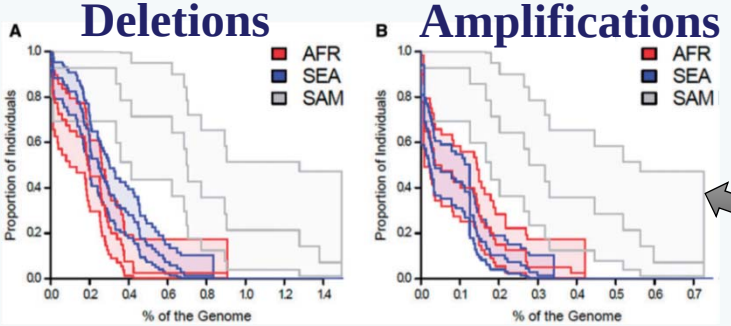
Eastman et al., Antimicrob. Agents Chemother., 2011

Piperaquine resistance is associated with a CNV on chr 5

Piperaquine + **dihydroartemisinin** has recently become the official first-line therapy in several ***Southeast Asian*** countries.



Cheeseman et al., Mol. Biol. Evol., 2016



Malaria

CNVs were significantly more common in South America

CNVs show **diverse genetic distributions** in **geographically dispersed populations**

Motivation 1

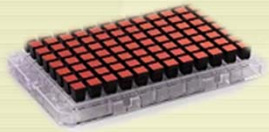
Genotyping solution

population -specific + *cost-effective*

- *GWAS*
- *CNVs*

*Array 6.0 vs. Axiom TWB

(350,075/95 = 3685 TWD/sample)



New-Generation Population-Optimized Human Arrays:

Affymetrix Axiom genotyping solution

The study highlights the potential uses of Axiom genotyping solution prevalent in tropical infectious diseases

Axiom_aegypti1

G3·Genes | Genomes | Genetics

INVESTIGATION

A Multipurpose, High-Throughput Single-Nucleotide Polymorphism Chip for the Dengue and Yellow Fever Mosquito, *Aedes aegypti*

Benjamin R. Evans,*,[1] Andrea Gloria-Soria,* Lin Hou,† Carolyn McBride,‡ Mariangela Bonizzoni,§ Hongyu Zhao,† and Jeffrey R. Powell*

*Department of Ecology and Evolutionary Biology, Yale University, New Haven, Connecticut 06511, †Department of Biostatistics, Yale School of Public Health, New Haven, Connecticut 06520, ‡Princeton Neuroscience Institute and Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey 08540, and §Department of Molecular Biology and Biochemistry, University of California Irvine, Irvine, California 92697

Major vector of dengue and yellow fever viruses

Motivation 2

Axiom array was originally developed for genotyping

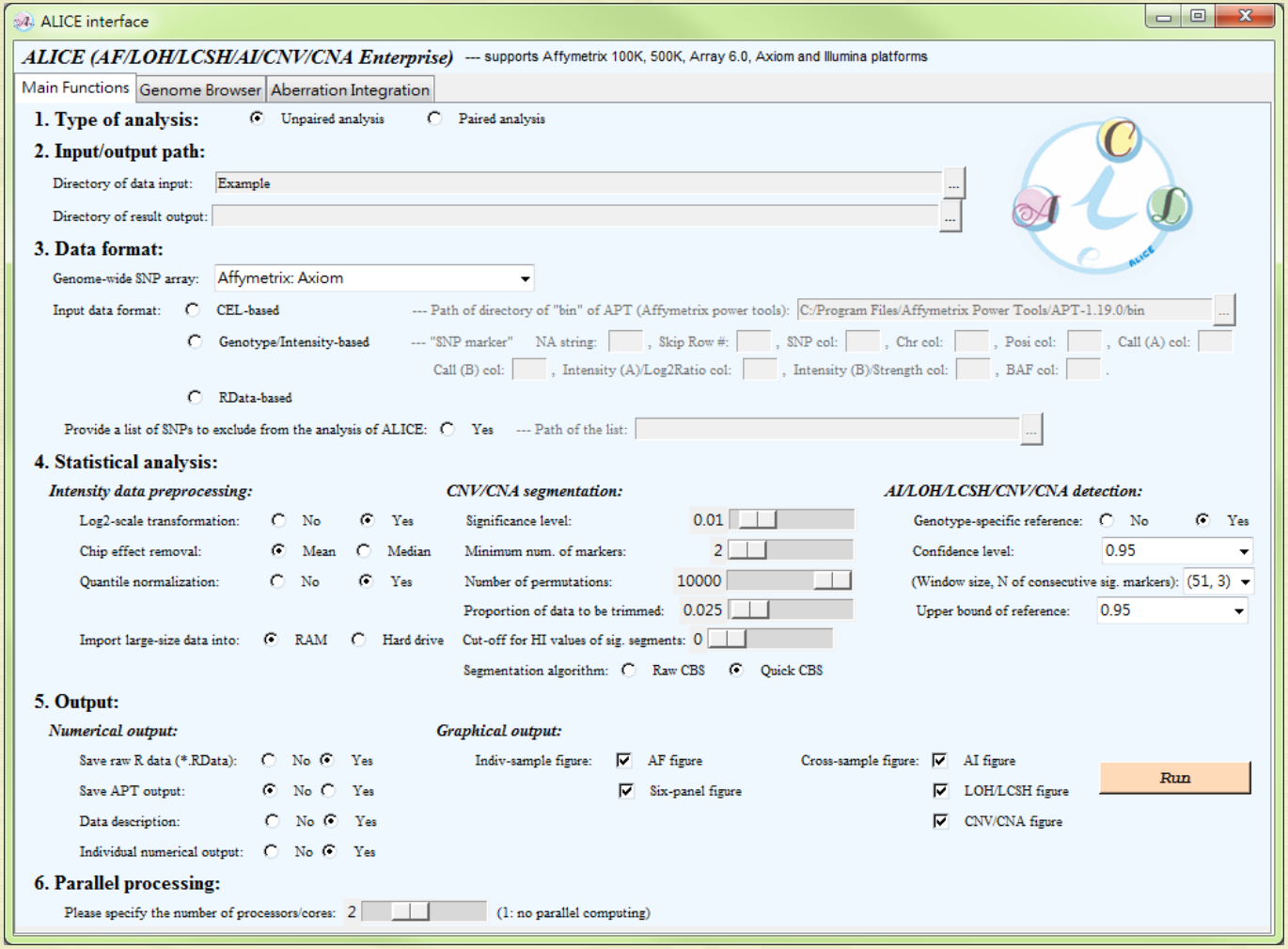
CNV

No public software is available

for the **integrated** genomic analysis of **hybridization intensities** and **genotypes** for this new-generation population-optimized genotyping platform

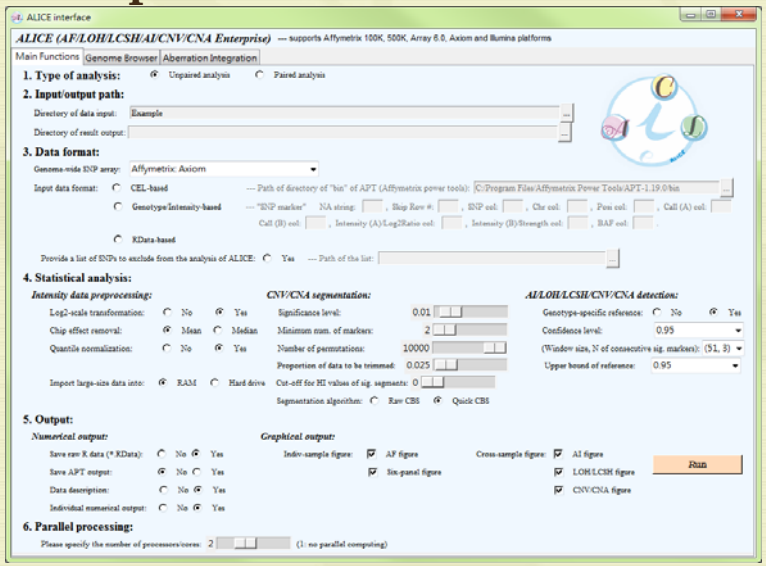
an integrated genomic analysis **software**

ALICE (AF/LOH/LCSH/AI/CNV/CNA Enterprise) software

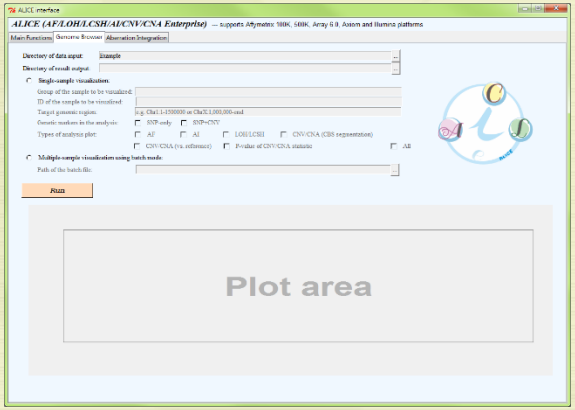


Three main components of ALICE

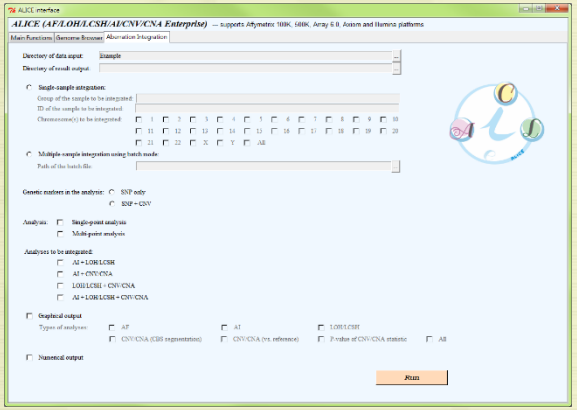
Component 1: "Main Functions."



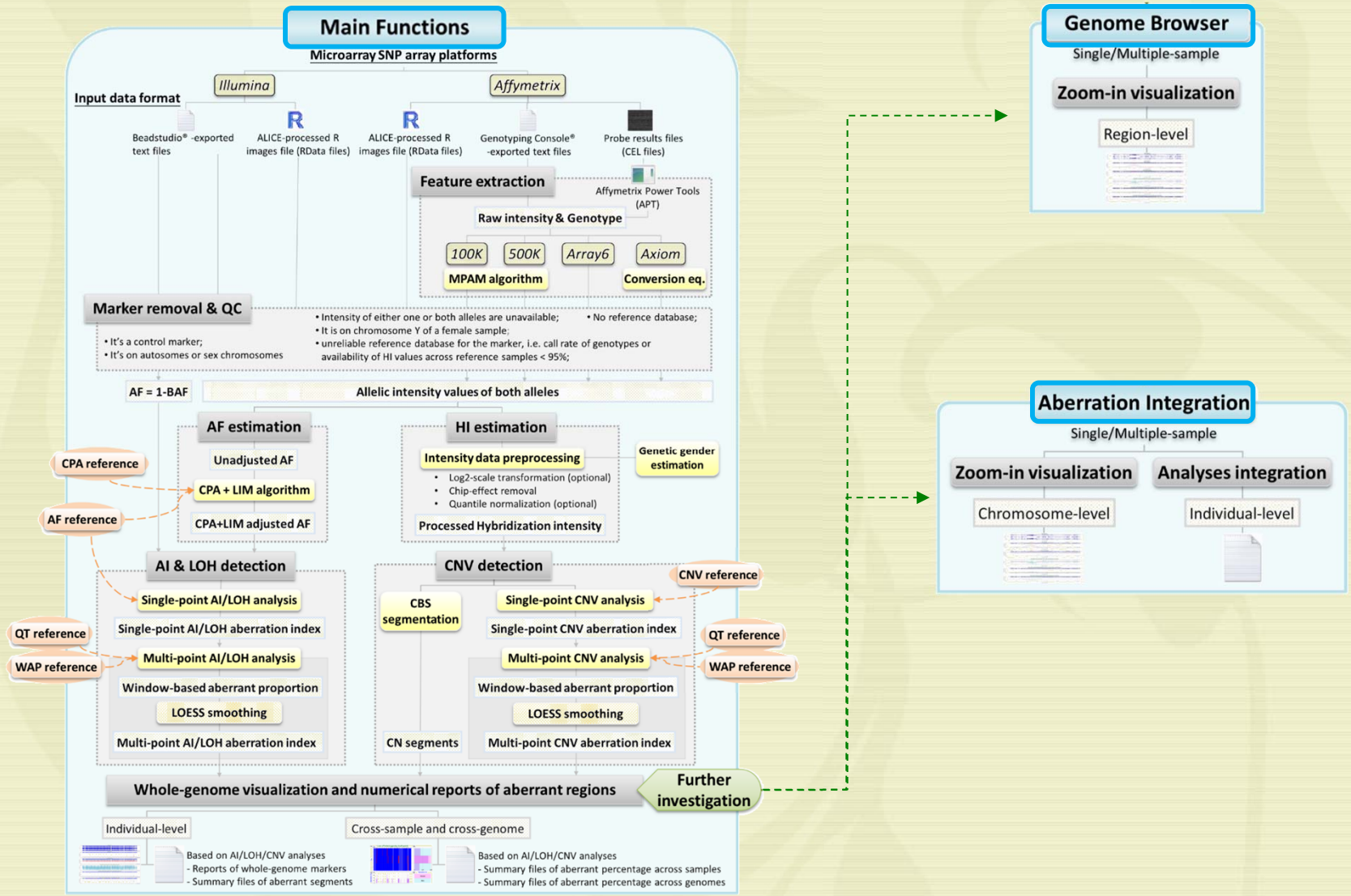
Component 2: "Genome Browser."



Component 3: "Aberration Integration."



The structure of ALICE software



Methods for the integrated genomic analysis

- **Extraction of HI**
  - $\begin{cases} h_A = 2^{S+0.5L} \\ h_B = 2^{S-0.5L} \end{cases}$ where S: Strength, L: Log_2 ratio
- **Preprocessing of HI**
  - $t_m = s_m - \frac{\sum_{i=1}^{M} s_i \cdot I[\Delta_i]}{\sum_{i=1}^{M} I[\Delta_i]}$
- **AF estimation with a CPA + LIM adjustment**
  - (1) CPA adjustment
    - $\hat{h}_{i,m} = \frac{h_{i,m}}{h_{i,m} + \kappa_m \cdot (1 - h_{i,m})}$
    - where $\kappa_m = \frac{1}{n_m(AB)} \sum_{i=1}^{n_m(AB)} \frac{h_{i,m}}{1-h_{i,m}} + \frac{n_m(AB)}{n_m(AB)-1} \left[\frac{\sum_{i=1}^{n_m(AB)} h_{i,m}}{1 - \sum_{i=1}^{n_m(AB)} h_{i,m}} - \frac{1}{n_m(AB)} \sum_{i=1}^{n_m(AB)} \frac{h_{i,m}}{1-h_{i,m}} \right]$
  - (2) LIM adjustment
    - $\hat{f}_{i,m} = \begin{cases} 1, & \text{if } \bar{h}_{+,m}(AA) < \hat{h}_{i,m} \\ \frac{1}{2} + \frac{1}{2} \cdot \frac{\hat{h}_{i,m} - \bar{h}_{+,m}(AB)}{\bar{h}_{+,m}(AA) - \bar{h}_{+,m}(AB)}, & \text{if } \bar{h}_{+,m}(AB) < \hat{h}_{i,m} \le \bar{h}_{+,m}(AA) \\ \frac{1}{2} \cdot \frac{\hat{h}_{i,m} - \bar{h}_{+,m}(BB)}{\bar{h}_{+,m}(AB) - \bar{h}_{+,m}(BB)}, & \text{if } \bar{h}_{+,m}(BB) < \hat{h}_{i,m} \le \bar{h}_{+,m}(AB) \\ 0, & \text{if } \hat{h}_{i,m} \le \bar{h}_{+,m}(BB) \end{cases}$
- **Single-point index of AI detection**
  - $\bar{f}_{+,m}(g) = \frac{1}{n_m(g)} \sum_{i=1}^{n_m(g)} \hat{f}_{i,m}$
  - $S_{+,m}(g) = \left[\frac{1}{n_m(g)-1} \sum_{i=1}^{n_m(g)} \left(\hat{f}_{i,m} - \bar{f}_{+,m}(g) \right)^2 \right]^{1/2}$
  - $\begin{cases} CI_{+,m}^{\mathcal{A},SP}(AA) = \left[\bar{f}_{+,m}(AA) - Z_{1-\frac{\alpha}{3M}} \cdot S_{+,m}(AA), 1 \right] \\ CI_{+,m}^{\mathcal{A},SP}(AB) = \left[\bar{f}_{+,m}(AB) - Z_{1-\frac{\alpha}{6M}} \cdot S_{+,m}(AB), \bar{f}_{+,m}(AB) + Z_{1-\frac{\alpha}{6M}} \cdot S_{+,m}(AB) \right] \\ CI_{+,m}^{\mathcal{A},SP}(BB) = \left[0, \bar{f}_{+,m}(BB) + Z_{1-\frac{\alpha}{3M}} \cdot S_{+,m}(BB) \right] \end{cases}$
  - $I_{i,m}^{\mathcal{A},SP} = \begin{cases} 1, & \text{if } \hat{f}_{i,m} \notin CI_{+,m}^{\mathcal{A},SP}(AA), CI_{+,m}^{\mathcal{A},SP}(AB), \text{or } CI_{+,m}^{\mathcal{A},SP}(BB) \\ 0, & \text{otherwise} \end{cases}$
- **Single-point index of LOH/LCSH detection**
  - $CI_{+,m}^{L,SP}(AB) = \left[\bar{f}_{+,m}(AB) - Z_{1-\frac{\alpha}{2M}} \cdot S_{+,m}(AB), \bar{f}_{+,m}(AB) + Z_{1-\frac{\alpha}{2M}} \cdot S_{+,m}(AB) \right]$
  - $I_{i,m}^{L,SP}(AB) = \begin{cases} 1, & \text{if } \hat{f}_{i,m} \notin CI_{+,m}^{L,SP}(AB) \\ 0, & \text{otherwise} \end{cases}$
- **Single-point index of CNV/CNA detection**
  - $\bar{t}_{+,m}(g) = \frac{1}{n_m(g)} \sum_{i=1}^{n_m(g)} t_{i,m}$
  - $\hat{\sigma}_{+,m}(g) = \left[\frac{1}{n_m(g)-1} \sum_{i=1}^{n_m(g)} \left(t_{i,m} - \bar{t}_{+,m}(g) \right)^2 \right]^{1/2}$
  - $CI_{+,m}^{\mathcal{C},SP}(g) = \left[\bar{t}_{+,m}(g) - Z_{1-\frac{\alpha}{2M}} \cdot \hat{\sigma}_{+,m}(g), \bar{t}_{+,m}(g) + Z_{1-\frac{\alpha}{2M}} \cdot \hat{\sigma}_{+,m}(g) \right]$
  - $I_{i,m}^{\mathcal{C},SP}(g) = \begin{cases} 1, & \text{if } t_{i,m} > \bar{t}_{+,m}(g) + Z_{1-\frac{\alpha}{2M}} \cdot \hat{\sigma}_{+,m}(g) \\ -1, & \text{if } t_{i,m} < \bar{t}_{+,m}(g) - Z_{1-\frac{\alpha}{2M}} \cdot \hat{\sigma}_{+,m}(g) \\ 0 & \text{otherwise} \end{cases}$
  - $p_{i,m}^{\mathcal{C},SP} = \min \left\{ 2 \left(1 - \Phi \left(Z_{i,m}^{\mathcal{C},SP} \right) \right) \cdot M, 1 \right\}$ where $Z_{i,m}^{\mathcal{C},SP} = (t_{i,m} - \bar{t}_{+,m}) / \hat{\sigma}_{+,m}$ is the test statistic.
- **Multipoint indices of AI, LOH/LCSH, and CNV/CNA detection**
  - $W_{i,m}^{\mathcal{E},MP}(v, n_c) = \frac{1}{2v+1} \sum_{x \in \{m-v, m-v+1, \cdots, m, \ldots, m+v-1, m+v\}} J_{i,x}^{\mathcal{E},SP}$ where $J_{i,x}^{\mathcal{E},SP} = I[\sum_{l=1,\ldots,n_c} \prod_{z=x-n_c+l, x-n_c+l+1, \ldots, x+l-1} I_{i,z}^{\mathcal{E},SP} > 0]$
  - (1) Confidence interval method
    - Smoothed the WAPs using the local regression LOESS function for every sample: $\widetilde{W}_{i,m}^{\mathcal{E},MP}(v, n_c)$
    - Calculate the Q%-quantile of the smoothed WAPs from reference samples: $\tilde{Q}_{i,m}^{\mathcal{E},MP}(v, n_c)$
    - First multipoint detector: $I_{i,m}^{\mathcal{E},MP}(v, n_c, 1) = I\left[\widetilde{W}_{i,m}^{\mathcal{E},MP}(v, n_c) > \tilde{Q}_{i,m}^{\mathcal{E},MP}(v, n_c) \right]$
  - (2) LIM adjustment
    - Calculate the mean and standard deviation of the WAP statistics for $\mathcal{E}$ for all the normal reference samples: $\hat{\mu}_{i,m}^{\mathcal{E},MP}(v, n_c)$ and $S_{i,m}^{\mathcal{E},MP}(v, n_c)$
    - Calculate the test statistic: $Z_{i,m}^{\mathcal{E},MP}(v, n_c) = \frac{W_{i,m}^{\mathcal{E},MP}(v, n_c) - \hat{\mu}_{i,m}^{\mathcal{E},MP}(v, n_c) + \frac{1}{M}}{S_{i,m}^{\mathcal{E},MP}(v, n_c)}$
    - Calculate the adjusted p value after Bonferroni correction: $p_{i,m}^{\mathcal{E},MP}(v, n_c) = min\{ [1 - \Phi(Z_{i,m}^{\mathcal{E},MP}(v, n_c))] \cdot M, 1 \}$
    - Second multipoint detector: $I_{i,m}^{\mathcal{E},MP}(v, n_c, 2) = I\left[p_{i,m}^{\mathcal{E},MP}(v, n_c) < 0.05 \right]$

    In a real data analysis, we consider their combination $I_{i,m}^{\mathcal{E},MP}(v, n_c) = I_{i,m}^{\mathcal{E},MP}(v, n_c, 1) \times I_{i,m}^{\mathcal{E},MP}(v, n_c, 2)$
- **Quick-CBS algorithm**
  - $d_{i,m}^{\mathcal{E}} = W_{i,m}^{\mathcal{E},MP}(v, n_c) - Q_{i,m}^{\mathcal{E},MP}(v, n_c)$ ➔ $\tilde{d}_{i,m}^{\mathcal{E}} = 2 \cdot \frac{d_{i,m}^{\mathcal{E}} - c_{i,min}^{\mathcal{E}}}{c_{i,max}^{\mathcal{E}} - c_{i,min}^{\mathcal{E}}} - 1$
  - The weight for the m^{th} SNP of the i^{th} individual is calculated as follows: $\widetilde{w}_{i,m} = \frac{w_{i,m}}{\sum_{m=1}^{M} w_{i,m}}$
  - where $w_{i,m} = 10^{-10} + max\{\tilde{d}_{i,m}^{\mathcal{A}}, \tilde{d}_{i,m}^{L}\} \cdot I\left[max\{\tilde{d}_{i,m}^{\mathcal{A}}, \tilde{d}_{i,m}^{L}\} > 0 \right]$
  - A *weighted t test* statistic based on weight $\widetilde{w}_{i,m}$ is used to analyze the difference in the averages of two segments in a region of AI or LOH/LCSH.
  - A permutation test, which randomly shuffles the data in two segments, is used to calculate an empirical p value.

Visualization of the integrated analysis results 1

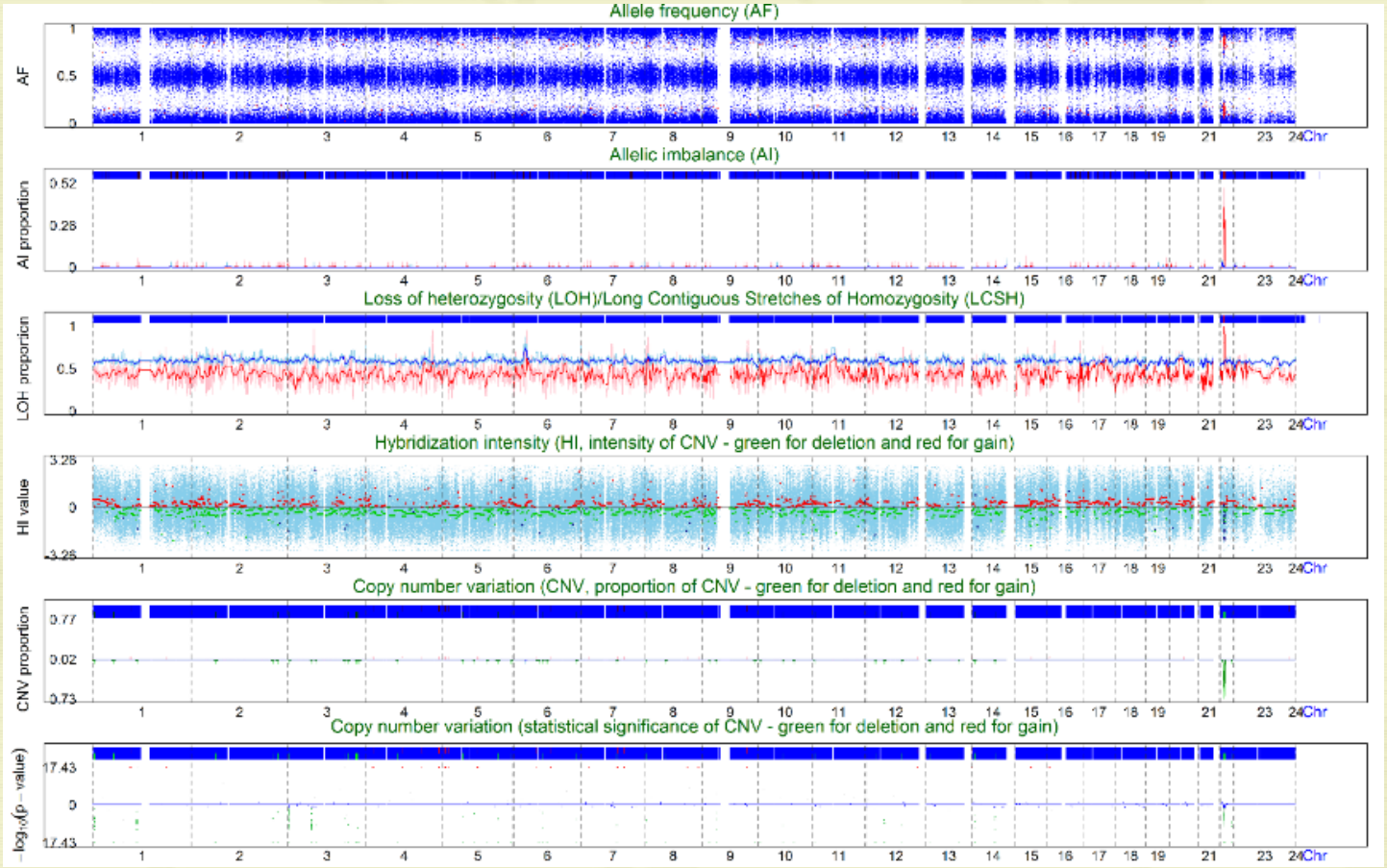
A normal sample

AF

AI

LOH/ LCSH

CNV/ CNA



Visualization of the integrated analysis results 2

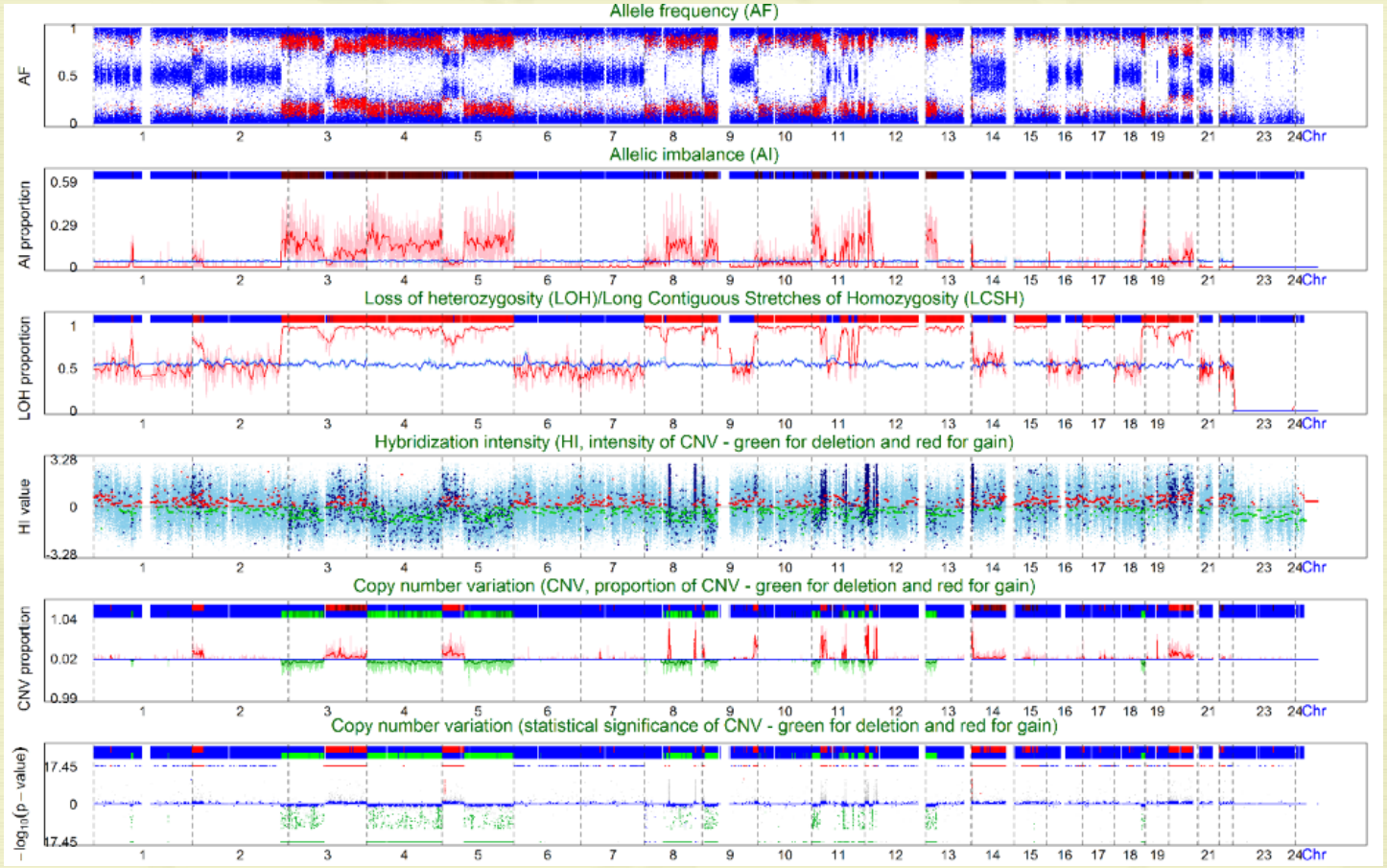
A tumor sample

AF

AI

LOH/ LCSH

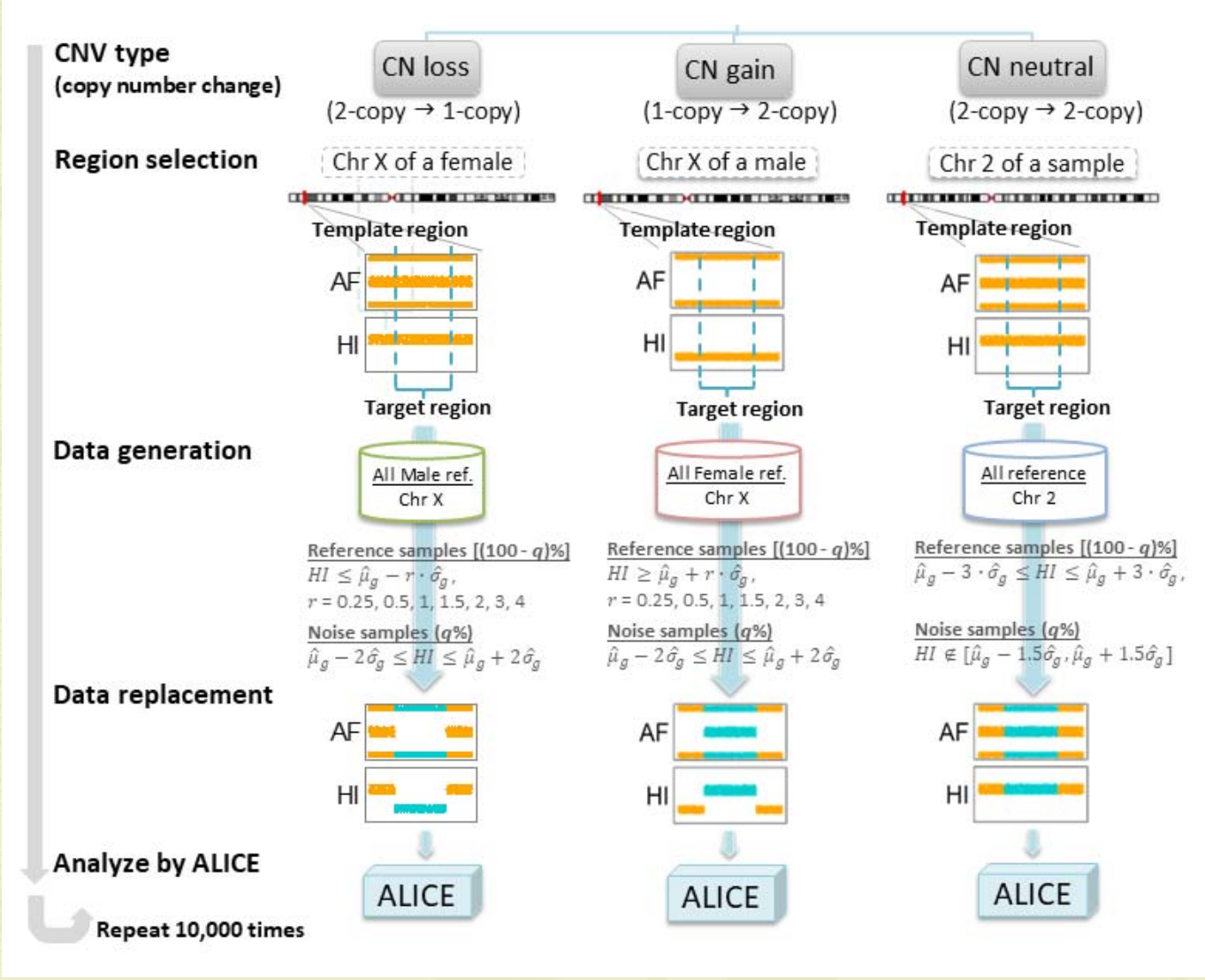
CNV/ CNA



Evaluation of the performance

- Simulation study
- Real data analysis
- Validation using qPCR experiment
- Quick-CBS algorithm

Evaluation of the performance: based on **Simulation study**



Performance of the CNV/CNA analysis using ALICE

Level of noise interference	Suggested setting (w, n_c)	FPR and TPR (Simulation scenario)	N(SNPs) in the target region			
			11	**51**	**101**	**501**
Without noise interference (q% = 0%)	(11, 2)	Average FPR (neutral)	1.12	1.12	1.12	1.12
		Average TPR (loss)	95.55	**94.08**	95.39	95.43
		Average TPR (gain)	**99.39**	96.69	95.59	95.83
With noise interference (q % = 25%)	(51, 3)	Average FPR (neutral)	2.19	2.19	2.19	2.19
		Average TPR (loss)	42.09	**85.45**	**94.03**	93.54
		Average TPR (gain)	50.67	89.37	92.81	93.55

The proposed **CNV/CNA detection**,

which integrates **AI** and **LOH/LCSH** detection,

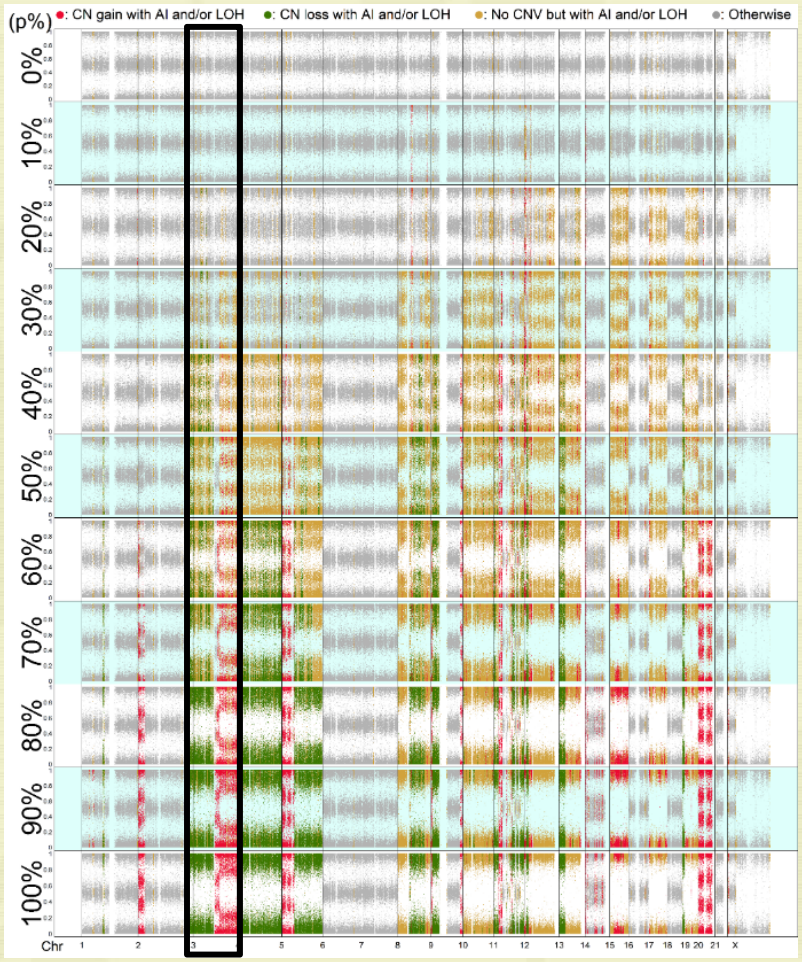
had a **promising *TPR*** and **well-controlled FPR** in simulation studies.

Evaluation of the performance: based on **Real data analysis**

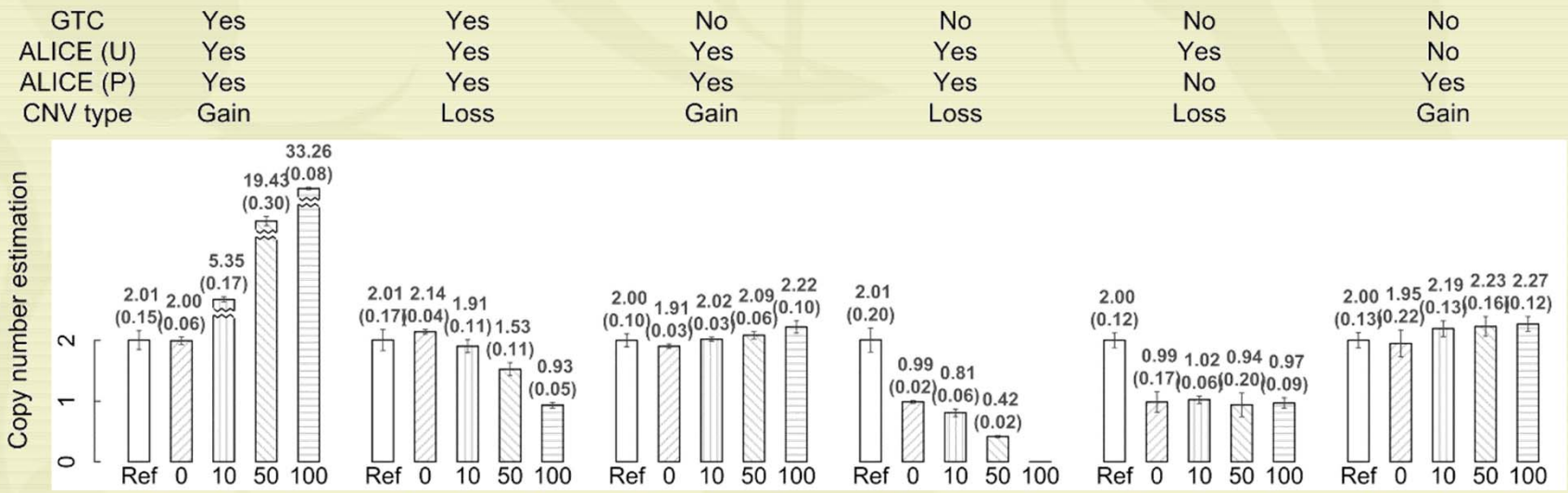
We analyzed **3,236 samples** genotyped using different platforms

- **3, 235** unrelated noncancerous samples
- **11 admixed samples**
  based on 1 lung cancer patient

Dynamic patterns of whole-genome *AF* plot



Evaluation of the performance: based on **qPCR experiment**



	Region 1	Region 2	Region 3	Region 4	Region 5	Region 6
	Chr 8	Chr 2	Chr 4	Chr 15	Chr 6	Chr 14
qPCR primer	[128,548,712 bp, 128,548,812 bp]	[228,813,220 bp, 228,813,320 bp]	[93,980,487 bp, 93,980,667 bp]	[71,630,915 bp, 71,631,015 bp]	[67,025,247 bp, 67,025,321 bp]	[95,137,294 bp, 95,137,444 bp]
ALICE	[128,539,148 bp, 128,563,712 bp]	[228,803,376 bp, 228,825,101 bp]	[93,859,694 bp, 94,013,938 bp]	[71,610,835 bp, 71,632,750 bp]	[66,999,646 bp, 67,033,086 bp]	[95,129,190 bp, 95,147,310 bp]

The results **successfully validated** the CNVs/CNAs identified in the Axiom data analyses using the proposed methods

ALICE website

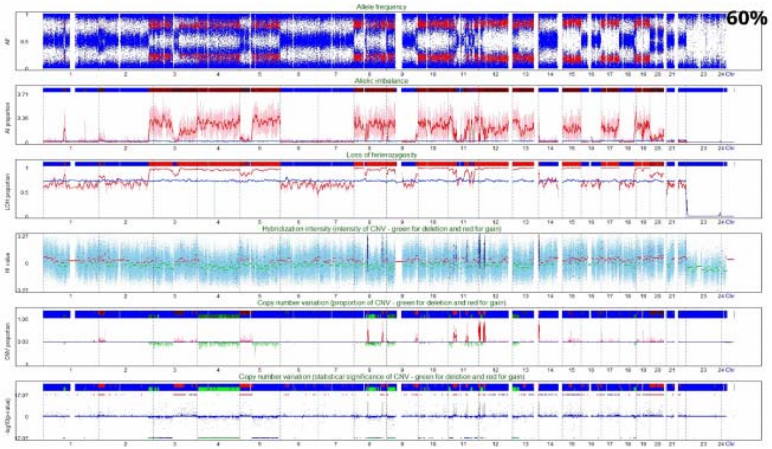
http://hcyang.stat.sinica.edu.tw/software/ALICE.html

Alice (AF/LOH/LCSH/AI/CNV/CNA Enterprise)

Announcement (2016-10-01):
To fulfill the requirements of different Axiom SNP arrays and laboratories, we can provide customized reference databases of ALICE for you. If you have the need, please email Dr. Hsin-Chou Yang (hsinchou@stat.sinica.edu.tw).

Introduction:

ALICE (AF/LOH/LCSH/AI/CNV/CNA Enterprise) is user-friendly software for an integrated analysis of allele frequency (AF), allelic imbalance (AI), loss of heterozygosity (LOH), long contiguous stretch of homozygosity (LCSH), and copy number variation or alteration (CNV/CNA) on the basis of SNP probe hybridization intensities and genotypes. The software, user manual, library files for APT, annotation files, test examples, and reference databases can be downloaded below.



Download software & user manual:

Version	Content	Screen resolution	Architecture	Size	Update date
ALICE v. 1.0	Software	Width < 800	32-bit	164 MB	2015/10/04
			64-bit	164 MB	2015/10/04
		Width ≥ 800	32-bit	164 MB	2015/10/04
			64-bit	164 MB	2015/10/04
	User manual - a brief guide for running a default example in ALICE			1.07 MB	2015/10/04
	User manual - a full guide for all functions in ALICE			5.30 MB	2015/10/04
	Frequently asked questions			349.5 KB	2015/10/04

* We provide a default example in the ALICE software. Therefore, the file is somewhat large!

Download library files for Affymetrix Power Tools (APT):

Affymetrix Platform	100K	500K	Array 6.0	Axiom (CHB 1)
File Size	19.6 MB	65.2 MB	79.8 MB	73.9MB
Original resource	Hind, Xba	Nsp, Sty	Array6	Axiom CHB1

Download annotation files:

For Affymetrix:

Version	na28 (hg18/dbSNP 128)	na29 (hg18/dbSNP 128)	na30 (hg18/dbSNP 128)	na31 (hg19/dbSNP 131)	na32 (hg19/dbSNP 132)	na33 (hg19/dbSNP 137)
100K	na28	na29	na30	na31	na32	
500K	na28	na29	na30	na31	na32	
Array 6.0	na28	na29	na30	na31	na32	na33
Axiom					na32	na33

For Illumina:
HumanHap550v3_B.csv

Download examples:

Example	1-1	1-2	1-3	2-1	2-2	2-3	3-1	3-2
Batch					Batch	Batch		
File size	390 MB	189 MB	189 MB	172 MB	147 MB	150 MB	219 MB	219 MB

Popultaion	Support platform	Input data format	Sample size	Parameter (w, nc)	Database index 1	2	3	4	5	6	7	8
Combined (CEU + CHB + JPT + YRI)	Affymetrix 100K	GTC-exported text file	210	(11, 1)								
				(51, 3)								
				(1001, 5)								
	Affymetrix 500K	GTC-exported text file	210	(11, 1)								
				(51, 3)								
				(1001, 5)								
	Affymetrix Array 6.0	Probe results file (*.CEL)	210	(11, 1)								
				(51, 3)								
				(1001, 5)								

Reference (* correspondence author):

Mei-Chu Huang, Tze-Po Tsuang, Chien-Hsiun Chen, Jer-Yuarn Wu, Yuan-Tsong Chen, Ling-Hui Li*, and Hsin-Chou Yang* (2015) An Integrated Analysis Tool for Analyzing Hybridization Intensities and Genotypes Using New-Generation Population-Optimized Human Arrays. BMC Genomics 17:266. (http://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-016-2478-8)

ALICE paper: Huang et al., *BMC Genomics*, 2016

Huang *et al. BMC Genomics* (2016) 17:266
DOI 10.1186/s12864-016-2478-8

BMC Genomics

RESEARCH ARTICLE Open Access

An integrated analysis tool for analyzing hybridization intensities and genotypes using new-generation population-optimized human arrays

Mei-Chu Huang[1,2,3], Tzu-Po Chuang[4,5], Chien-Hsiun Chen[6], Jer-Yuarn Wu[6], Yuan-Tsong Chen[6], Ling-Hui Li[6*] and Hsin-Chou Yang[1,2,7,8,9,10*]

Dr. Yang

Dr. Li

Welcome for collaboration

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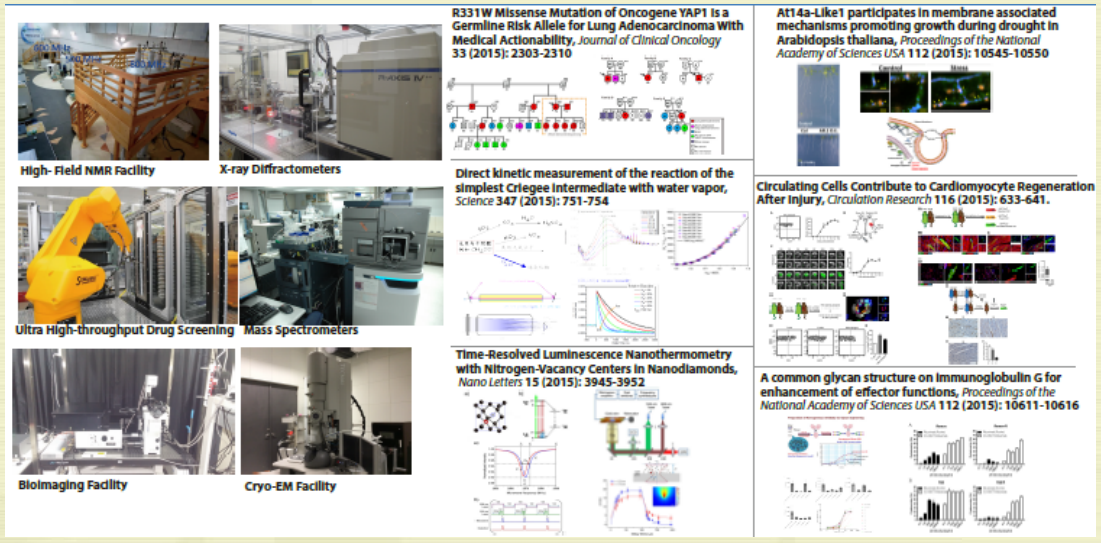
- 3 main divisions in Academia Sinica, division of Mathematics and Physical Science, life science and humanities and social science. Totally, 24 research institutes and 7 research centers
- 7900+ researchers and students from Taiwan and abroad



TIGP-
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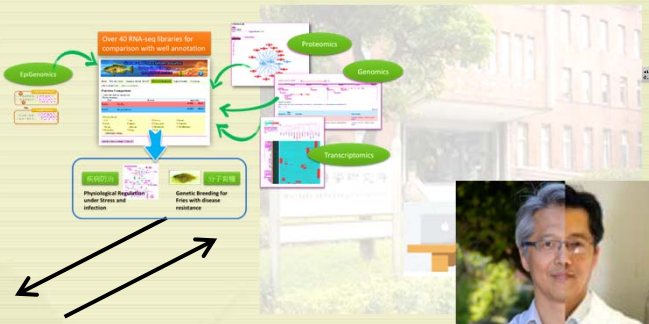
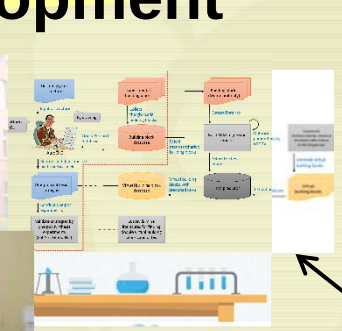
Institute of Information Science, Academia Sinica

TIGP BP

http://tigpbp.iis.sinica.edu.tw/tigpbio

Algorithm and Computational Method Development

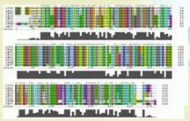




Interdisciplinary Collaboration

Dry/Wet Bioinformatian

Biological/Medical Studies



Computational Biology

Bio knowledge management

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Thank you very much for the attention.

Questions?