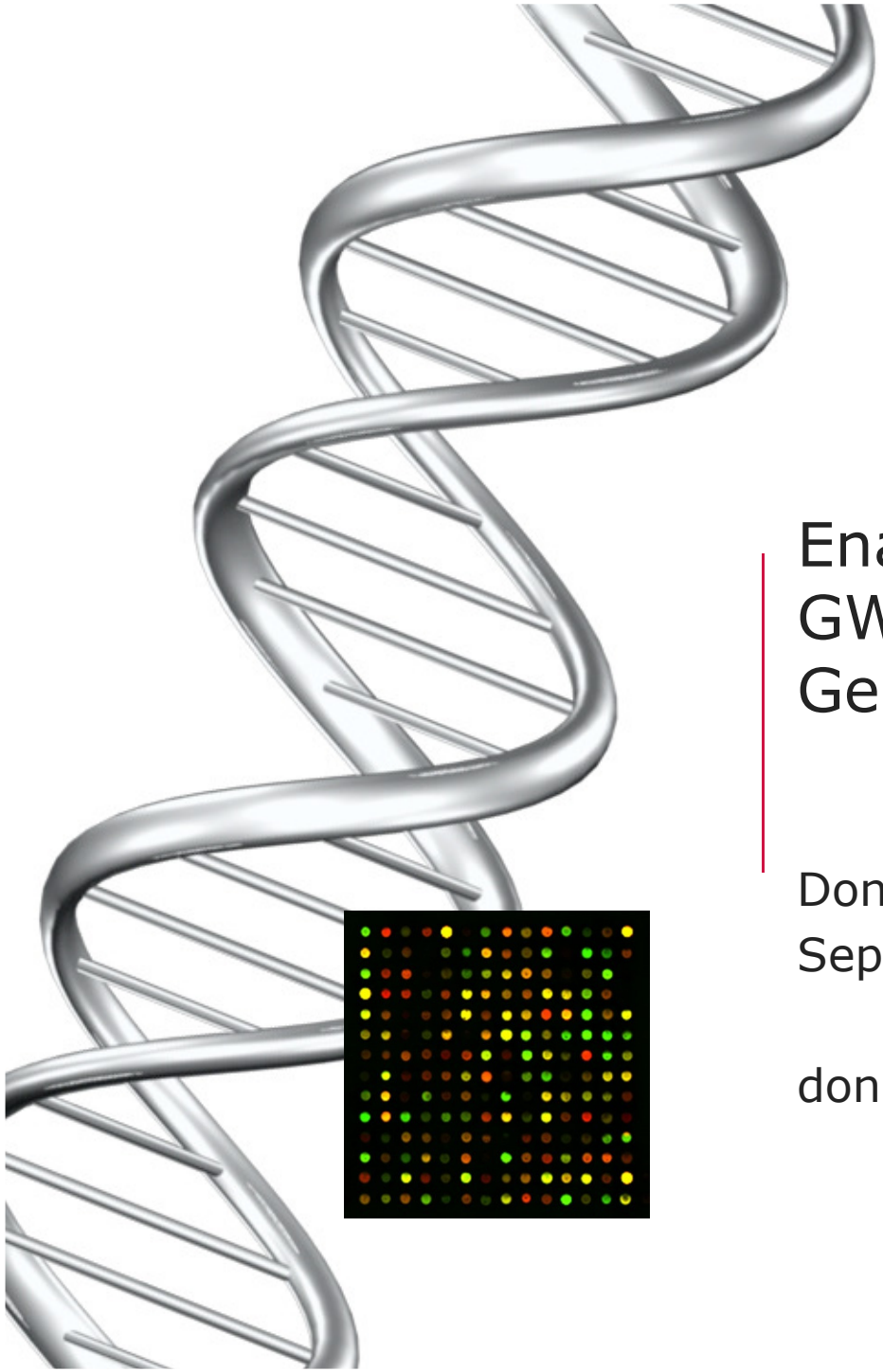

Enabling the Next Wave of GWAS with the Axiom™ Genotyping Solution

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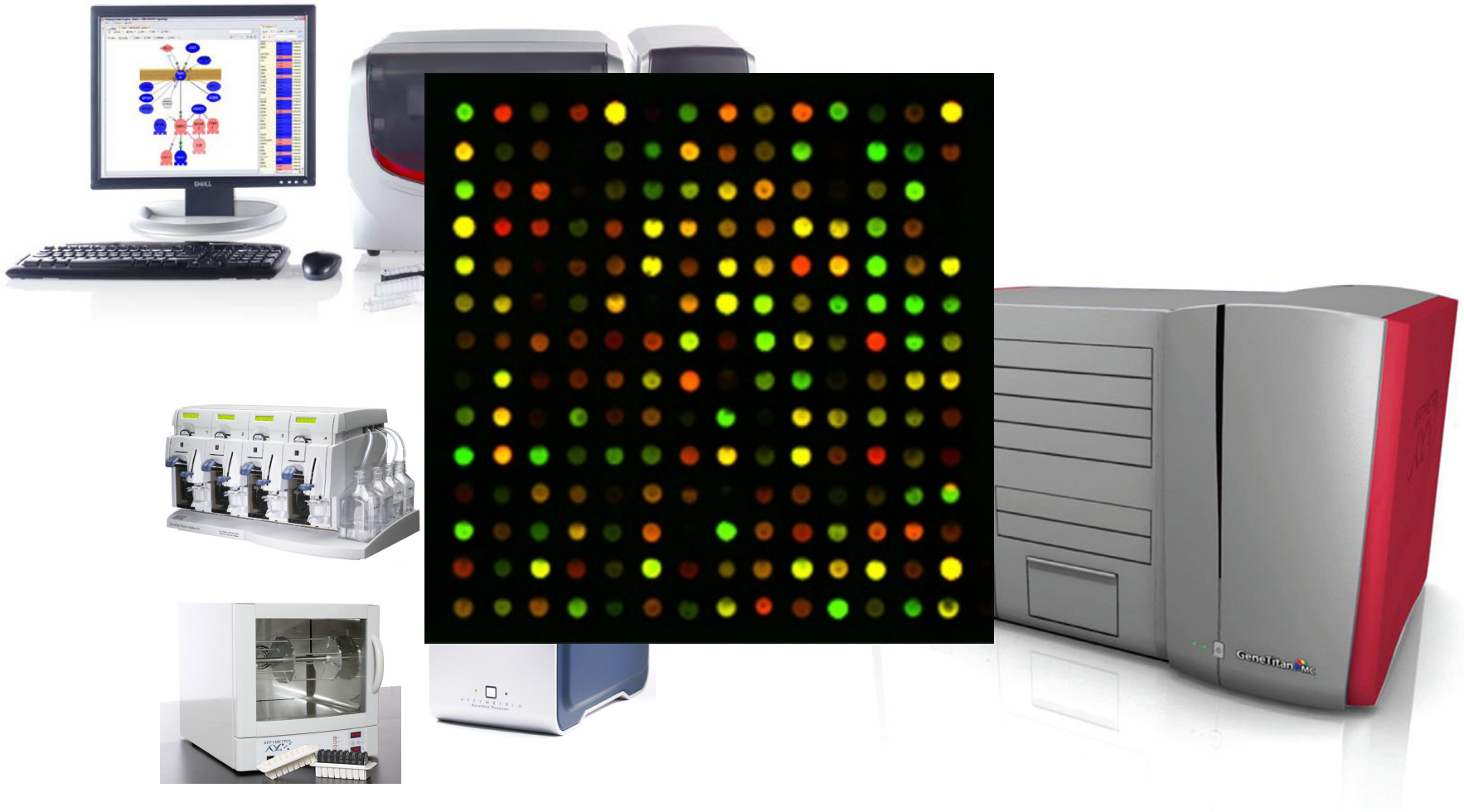
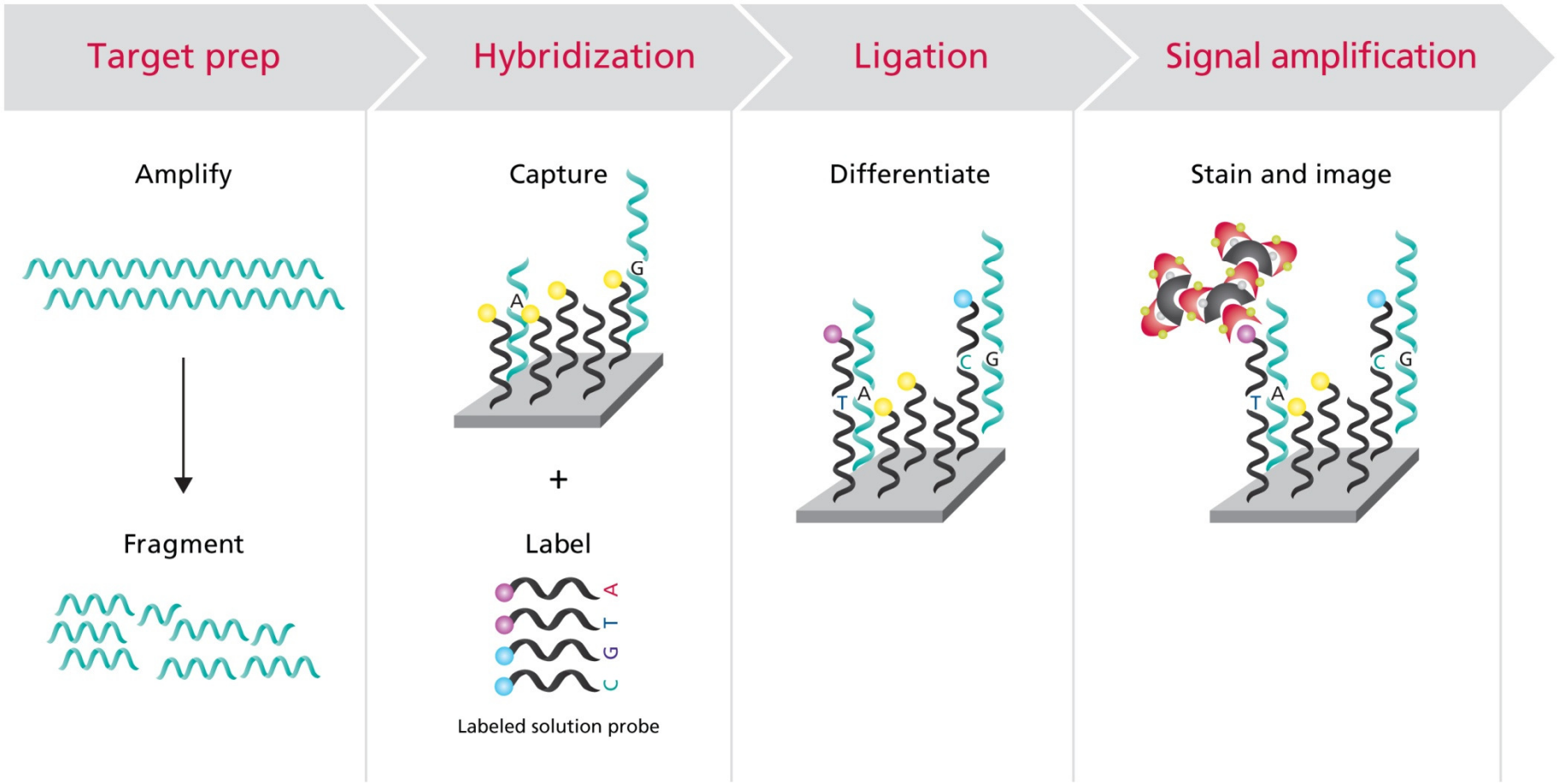
Current Affymetrix Platforms



A new ligation-based assay format offers robust & reliable results



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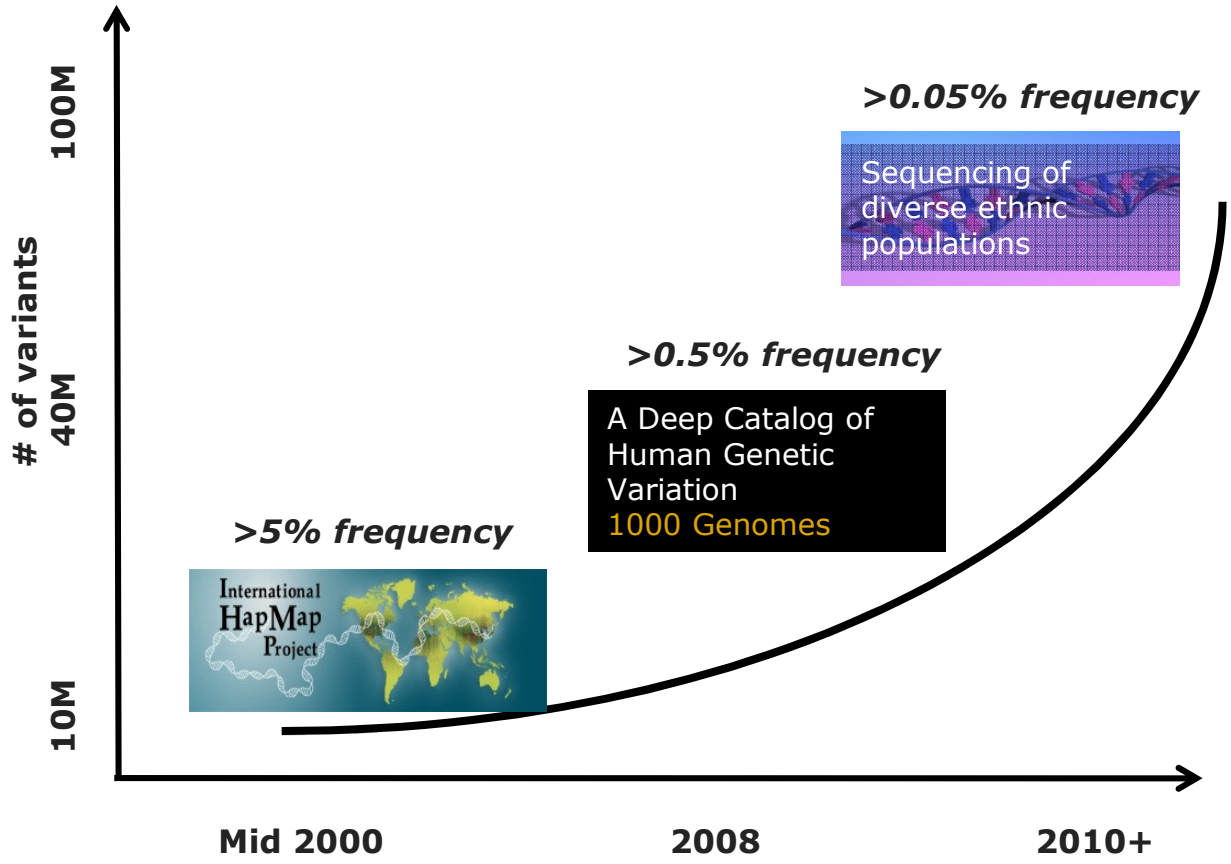
An expanded catalog of human variation will accelerate GWAS

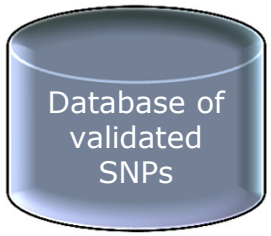
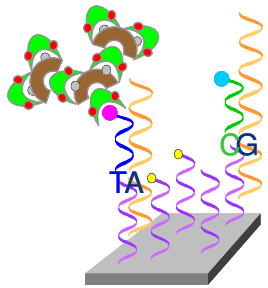
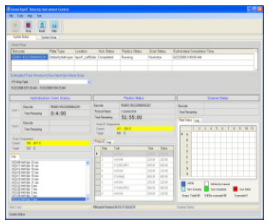


- Discovery initiatives may yield 10X more genetic variants
- A new approach to analyzing and studying genetic diversity
- Incorporating rare alleles (>0.05%) will require significant larger sample size

Introducing Affymetrix' new genotyping system for association studies

Axiom Genotyping Solution

A universally accepted principle or rule

					
AXIOM GENOMIC DATABASE	**AXIOM CUSTOM & CATALOG ARRAY PLATES**	**BECKMAN BIOMEK FX^P TARGET PREP EXPRESS**	**AXIOM™ REAGENT KIT**	**GENETITAN® SYSTEM**	**GENOTYPING CONSOLE™ SOFTWARE**
>11M validated common & rare variants	Up to 700k SNP's per array and up to 2.6M per sample	Automated target preparation*	New robust & reliable assay	Automated, hands-free array processing	Comprehensive user-friendly software suite

* Manual target prep protocol also available

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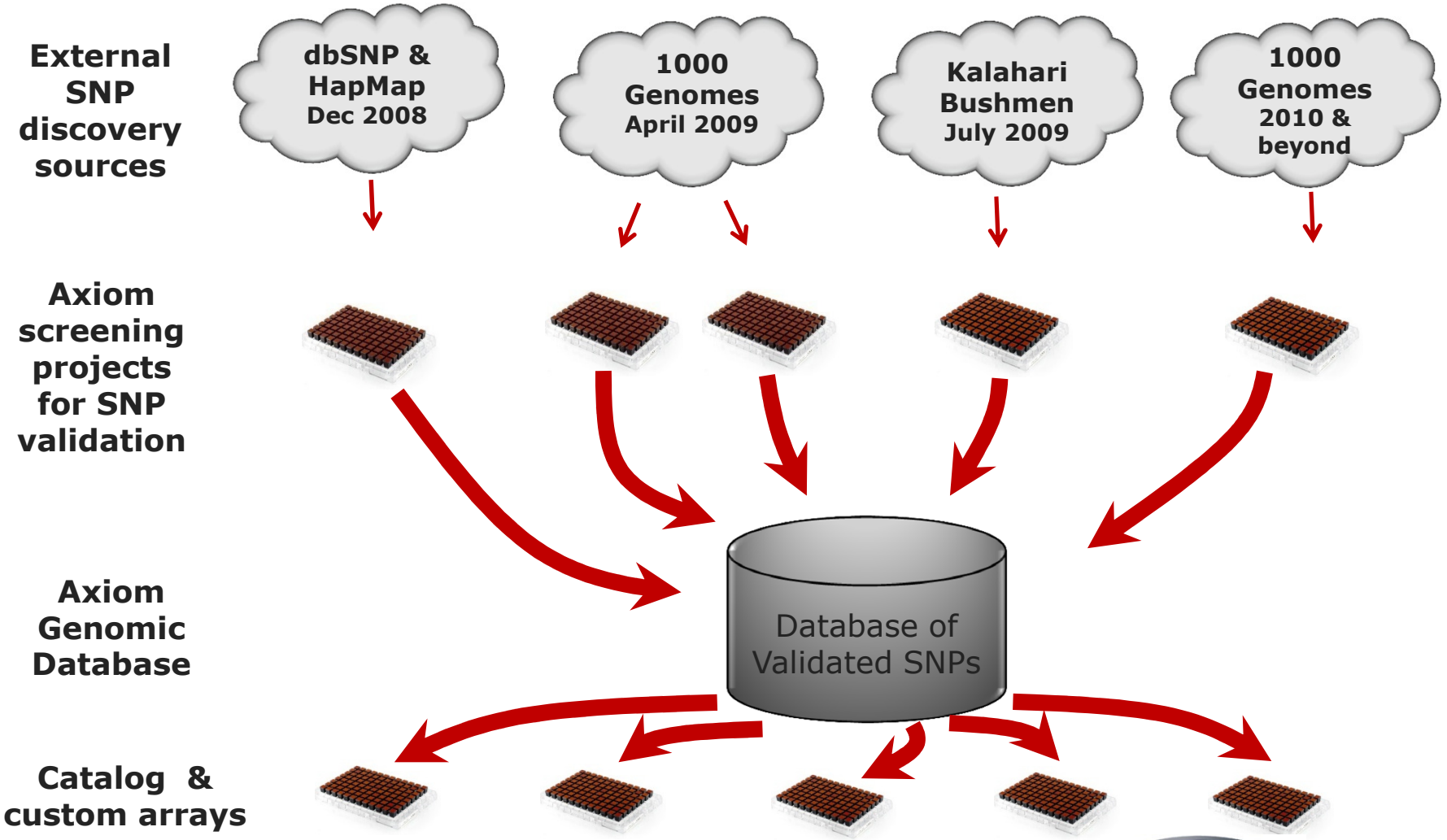
Axiom™ Genomic Database

Affymetrix has screened all publically available sources of human SNPs using Axiom



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Design Your Array Using Validated SNPs

Increase your chances of finding associations

Increase your chances of finding associations

- Validated SNPs are:
  - Markers that have been **reliably** genotyped for the **rare allele** in the Axiom™ assay
  - This means that it is shown to be polymorphic in the given population(s) by demonstrating reliable detection of minor allele
- Important to note: Sources of SNP discovery are known to be full of false positives
  - Can have false positive rates as high as 20%
  - Without validating each putative SNP, you don't easily know whether it's mono-morphic (i.e., not a real SNP) or simply did not work well in the assay

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Axiom™ Genotyping Solution: A comprehensive approach to association studies

Axiom Genotyping Solution

Array, Reagent Kit, Axiom Genomic Database, GeneTitan Instrument & Genotyping Console™ Software

Complete, scalable, and reliable solution for multiple genotyping applications

Axiom Genome-Wide Arrays

Axiom Genome-Wide Arrays (CEU, ASI, PanAFR & YRI)

Rapid and cost-effective solution for GWAS in single populations

Axiom myDesign™ Arrays

Axiom Genomic Database & Axiom myDesign Arrays

Tailored content for GWAS with new/diverse populations, replication, fine mapping, and candidate gene studies

Axiom Genomic Screening Service

Axiom Genomic Database Screen (5M marker screen)

Genome-wide, hypothesis-free screening against uncharacterized populations

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Affymetrix screened genomic content from several sources to develop the Axiom™ Genomic Database

Source	# screened	Pops
dbSNP HapMap*	3.6M	CEU, ASI, YRB
dbSNP non-HapMap	5.1M	CEU, ASI, YRB
1000 Genomes	5.2M	CEU, ASI
1000 Genomes	5.0M	YRI
KBM	1.7M	So. Afr., CEU, YRI and ASI
Total Screened	20.6M	

*Screened against HapMap 3 samples featuring 1,301 samples from 11 different populations

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Axiom™ myDesign™ Genotyping Array Plates are available in different configurations

96 samples	48 samples	24 samples
50K - 675K markers/sample	~1.3M markers/sample	~2.6M markers/sample

Choose your SNPs from the Axiom Genomic Database
or
add SNPs from your own database

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One FTE can support Axiom™ manual workflow

Monday

- Start DNA amplification on 3 plates of genomic DNA (plates A, B, and C)

Hands-on time: 2.5 hours

Tuesday

- Fragment and precipitate 2 plates (A & B) of amplified DNA
- Freeze plate C overnight

Hands-on time: 6 hours

Wednesday

- Re-suspend 2 plates (A & B) of precipitated DNA
- Fragment and precipitate plate C
- Begin hybridization on plate A

Hands-on time: 3 hours

Thursday

- Begin hybridization on plate B
- Re-suspend plate C
- Load GeneTitan® reagents for plate A
- Begin hybridization on plate C
- Begin scanning plate A

Hands-on time: 4 hours

Friday

- Load GeneTitan® reagents for plate B
- Load GeneTitan® reagents for plate C
- Begin scanning plates B & C

Hands-on time: 2 hours

1 full-time employee, <20 hours of hands-on time/week
3 plates/week x 96 arrays/plate = 288 samples/week
All hands-on time completed within 8-hour workday

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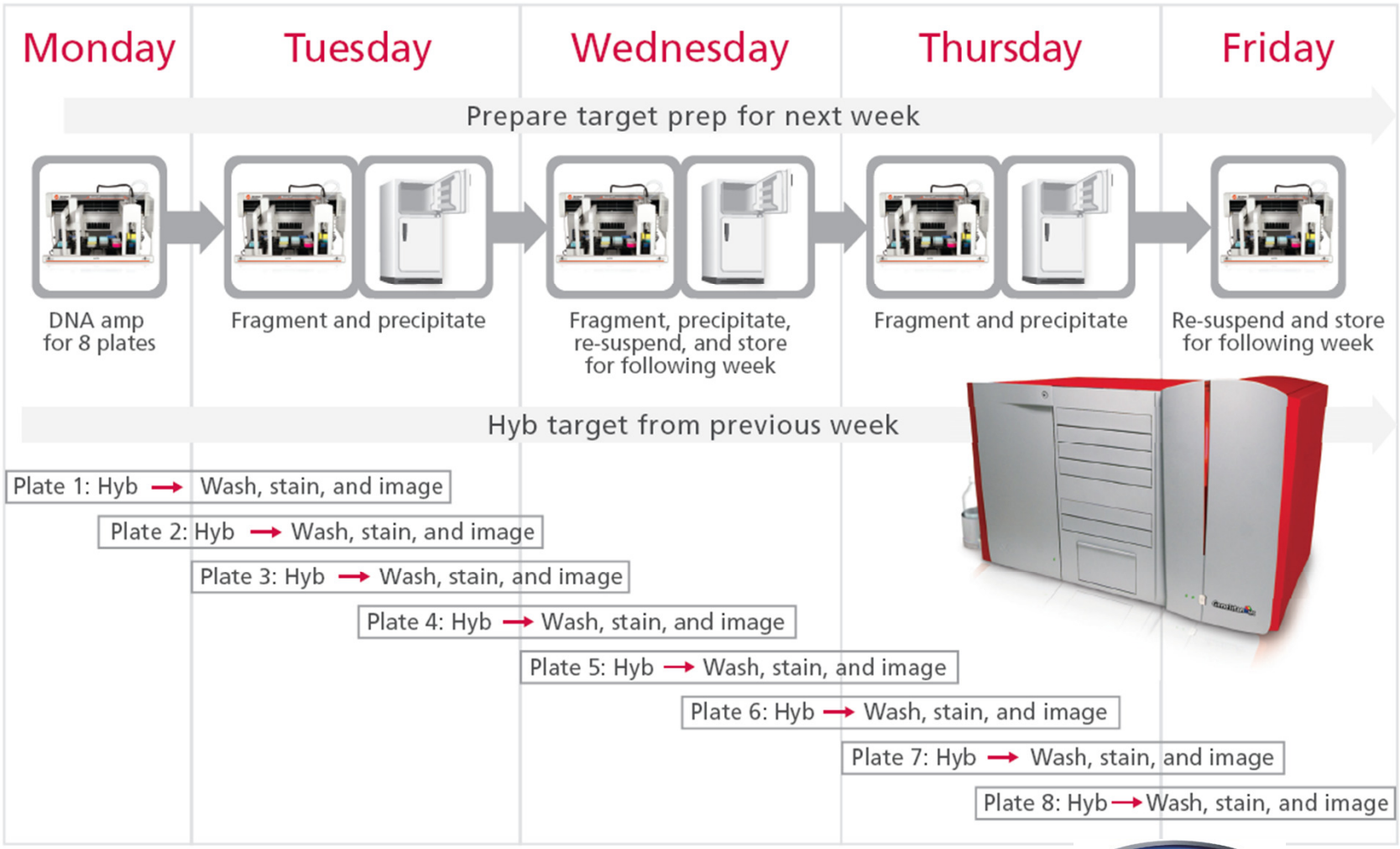
Axiom's high throughput workflow requires only 1.5 FTE's to maximize capacity

Achieve ~768 samples/week with 8 plate workflow



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Key features of Axiom™ myDesign™ Custom Arrays

Density	50K – 2.6M
Genome	Human
Applications	GWAS, replication, fine mapping, and candidate gene
Marker type	SNP and simple in/dels
Sources	Axiom Genomic Database De novo, target sequence
SNP selection	Manually by customer
SNP list submission	Online via myDesign NetAffx Workspace
Array design	Affymetrix Bioinformatics

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Axiom™ myDesign™ supports several design strategies

Leverage content from:

- Axiom Genomic Database
- De novo, target sequence

Fully customized

Design an entirely novel Axiom myDesign Array Plate with any density between 50,000 – 2.6 million markers per sample.

- Biological category (cSNPs, MHC, ADME)
- MAF (common, rare SNPs, or both)
- Population (CEU, etc.)
- Genomic region
- Commercially available panels (Affymetrix or ILMN)

Semi-customized

Supplement one of the currently available Axiom Genome-Wide Array Plates (CEU or ASI) with additional SNPs (up to 675K):

- Biological category
- MAF
- Population
- Genomic region

**Axiom YRI available in*

Semi-customized design: Supplementing an Axiom™ Genome-Wide Array

Axiom™ Genome-Wide CEU Array

- Includes 567K markers
- Supplement with additional 60,000 markers

Axiom™ Genome-Wide ASI Array

- Includes 598K markers
- Supplement with additional 40,000 markers

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Axiom™ myDesign™ Genotyping Arrays offer three major advantages

Comprehensive content

- Validated 1000 Genomes content
- Gene function
- Biological pathway
- Linkage disequilibrium
- Minor allele frequency
- Ethnic population

Flexible format

- Density: 50K – 2.6M SNPs array
- Scalable throughput
- Manual or automated workflow
- Supports GWAS, replication, and candidate gene studies

High quality

- Rigorous functional testing against HapMap
- High pass rate
- High call rate
- Highly reproducible

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Experimental workflow in human genomics

Discovery	SNP validation	Exploration	Replication	Fine mapping	Candidate gene	Routine test
Goal: Variant discovery	Biological validation	GWAS	Confirm GWAS hits	Identify causative	Confirm & correlate with disease phenotype	Diagnostic/ prognostic biomarker screening
Markers: 3 billion	>10 M	0.5M – 1M	200K – 500K	10K – 100K	100 – 5K	10 – 100s
Method: De novo sequencing	Custom screening arrays	Catalog or custom arrays	Custom arrays	Custom arrays	Custom array, RSQ, or RT-PCR	Custom array or RT-PCR
Sample size: 1-1,000	100s	1K – 100K	3K – 10,000	1K	100 – 1K	>100K
Sample type: Normals	Normals	Case-Control	Case-Control	Case-Control	Case-Control	Case

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A powerful combination

Axiom™ myDesign ™ Arrays with the Axiom Genomic Database

- Variety of relevant markers to help scientific discoveries
  - Optimize coverage for your population/cohort
  - Proven to work reliably; no need for optimization
  - Only pay for what you need
- Convenient and easy-to-design arrays with assistance from Bioinformatics Services
- Potential to leverage data sets from previous studies
- Superior data quality with exceptional sample pass rate, call rate, concordance, and reproducibility

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Conclusions on combining NGS with microarrays for validation & epidemiology

The combination of NGS (a powerful discovery tool for novel SNPs) and Axiom™ microarrays offers several distinct advantages over NGS alone.

Approach	Advantage	Disadvantage	Mitigation
Low-read-depth sequencing	Fast. Can sequence enough individuals to power epidemiology studies	High rate of false positives & error rate too high for epidemiology studies	Axiom™ myDesign™ Genotyping allows you to: ▪ Validate discovery ▪ Generate LD & MAF info on novel discovery ▪ Power your epidemiology studies faster and more cost effectively
High-read-depth sequencing	Lower false-positive error rate	Cannot cost-effectively and quickly sequence enough individuals to power epidemiology studies	

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Summary Notes

1. Affymetrix is a microarray-based solution to analysing GWAS pylomorphism
2. It is seen as a COMPLIMENTARY technology to NGS
3. Photo lithography allows for extremely high reproducibility of the array and precise concentration and sequences of probes
4. Ligation process allows for more stringent washes – high specificity
5. Affymetrix offers various solution platforms
    1. GCS3000 – single sample analysis, both expression & genotyping
    2. GeneATLAS – 4-sample analysis, expression analysis
    3. GeneTITAN – 96-sample and more analysis, both expression & genotyping
6. AXIOM offers both Catalogue as well as customised arrays ranging from 50k to 2.6M data points

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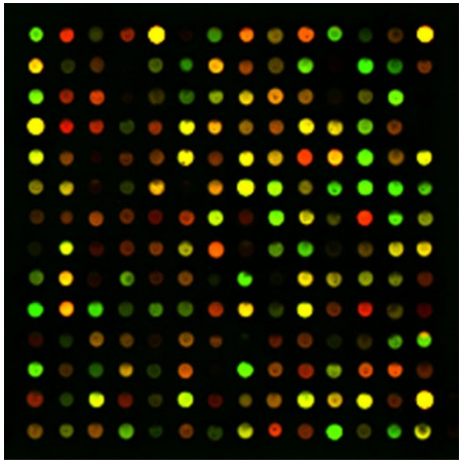

THANK YOU