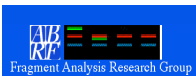


FARG 2006 Survey: A Comparative Study of the Methodology and Instrumentation Trends of Laboratories Performing DNA Genotyping

Katia Sol-Church¹ †, Doug Bintzler², Joe Forrester³, Robert Keefe⁴, Don Krist⁵, Christian Lytle⁶

¹ Nemours Children's Clinic, ² University of Cincinnati, ³ University of Missouri-Columbia, ⁴ Wadsworth Center/NYS DOH, ⁵ Rabin Med Center, ⁶ Dartmouth College,

† to whom correspondence should be directed



INTRODUCTION

The Fragment Analysis Research Group (FARG) conducted an on-line survey of laboratories performing DNA fragment analysis (FA), and genotyping studies. Previous FARG surveys (1999 and 2003) portrayed genotyping labs as small to mid-sized service operations, partially subsidized by home institutions. In these earlier periods, applications of emerging technologies to genotyping was already evident. Examples of those technologies are capillary-based electrophoresis, quantitative PCR, and mass spectrometry. The expanded options for genotyping reflected a broadening in the variety of types of genotyping being performed by laboratories that participated in those earlier surveys. In the 1990's, a lot of DNA FA focused on PCR amplification and characterizing simple sequence repeats (microsatellites), RFLPs or VNTRs. With the arrival of the genomics era, extensive DNA sequence databases became available to researchers hoping to examine other types of genetic differences amongst sample DNAs. This situation created a need for alternative methods for distinguishing genetic variability. In undertaking the current survey, the FARG proposed to examine whether, in the period between 2003 and 2006, the genotyping field experienced a shift in the types of technologies being used for FA. Additionally, it was of interest to assess how increased availability of many new platforms and chemistries for FA and genotyping influenced lab structure and functionality, i.e. how vendors who sell and provide the newer FA/genotyping technologies have affected the core lab. The goals of this survey, then, were threefold. First, to document the current status of genotyping facilities. Second, to note changes from previous surveys and, third, to obtain insights as to future directions in the FA field. The features of the facilities that were queried included: operation, staffing, funding, and equipment. The summarized survey results are reported here.

Methods & Study Design

The 2006 FARG survey was announced on the ABRF web site, Genome Technology and Electronic Discussion Group. The web based survey was posted at <http://surveymonkey.com/s.asp?u=630561261631>, and participants were requested to answer the 20 minute survey anonymously according to the service(s) they provided. The collected data was organized into 2 main sections:

- > A laboratory overview section collected general information on operation, staff and services.
- > The second section pertained specifically to the genotyping unit and investigated the types of applications, reagents and instrumentation used for fragment analysis and associated robotics.

Conclusions

Although inferences from a relatively small sample of respondents will require caution, a number of major trends appear in the data that are worth noting.

> **Response Sample:** 42 respondents represented labs from academic institutions (~60%), hospital-based labs (20%), government (5%), non-profit (5%), industry (5%), and "research group" (5%). Due to sampling bias (80% of the participating labs are also member of the ABRF), trends identified during this study will be most relevant to other core labs within this professional association.

> **Trends in the ABRF's Genotyping Lab Structure:** The core labs have diversified their services beyond mere FA. Currently, the services and support are offered for complementary areas such as proteomics, gene expression real time, microarray, and imaging. Interestingly, 35% of the polled labs received federal funding in 2006, compared to 23% in 2003.

> **Trends in Genotyping Services:** Although microsatellite (STR) has been for years the biomarker of choice, in the post genomic era SNPs have become progressively more widely utilized. 80% of the cores in our sample are currently using SNP as compared to 5% six years ago. This trend will probably continue, since 29% of respondents reported that they were planning to add new SNP services. Presently, new methods for mutation discovery (e.g. heteroduplex) are beginning to appear in a small minority of the laboratories.

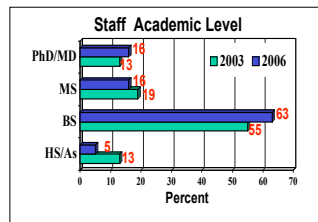
> **Major Technological Approaches:** Capillary electrophoresis is the platform of choice in core labs, though slab gels use persists at a lower level. Real time PCR appears as the rising star in genotyping labs and other technologies are emerging as complementary platforms (pyrosequencing, DHPLC, arrayed platforms and bioanalyzers).

> **Major Technology Platforms:** The ABI genetic analyzers are dominating in the sampling of core labs polled during this survey. However, alternative platforms and new manufacturers are appearing in this year's sampling of core labs: Real time PCR instruments (BioRad, and Roche), Licor systems, Biotage PSQ MA, Transgenomics WAVE, Beckman Coulter CEQ8000, Spectrumedix SCE9614, Illumina bead system, Affymetrix Chip, and Agilent 2100 bioanalyzer.

RESULTS: Survey of Laboratory

Figure 1: Staff / Laboratory Structure

The surveyed laboratories reported that the majority of lab personnel have been in their position less than three years [a], and that on average the numbers of PhD and BS have increased when compared to the number of MS [b]. Staff is also more likely to be hired as full time employees compared to in 2003 [c].



Funding Sources

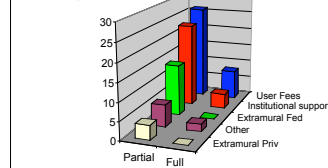


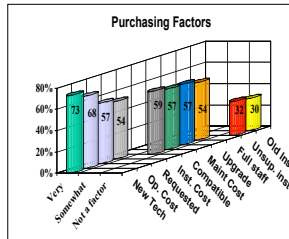
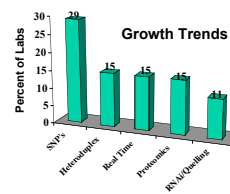
Figure 2: Funding

A total of 14 labs reported being fully funded with the majority of these lab funds coming from user fees. The remaining lab funds were from multiple sources with the top three being user fees, Institutional support and extramural funding from federal agencies. A few are supported by other funds such as corporate sponsorship or gifts.

Figure 3: Services found in genotyping labs

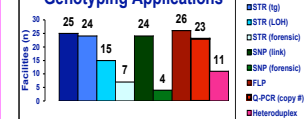
Equipment reported in our survey labs is what would be expected in labs working with DNA. DNA Sequencers, Thermo Cyclers, and spectrophotometers(a). 65% of lab say they are planning on offering new technologies to their labs. SNP studies out paced the Heteroduplex, RT-PCR, and Proteomic studies. When purchasing new equipment, the factors that are most important to the survey labs are adding new technologies and the operating costs of those technologies.

Equipment Numbers Reported	Microarrays	Chip Analy Inst	Oligo Syn	Cell culture	HPLC	2D gels	Mass Spec	Protein Syn
CE	35	31	30	27	26	22	13	11



RESULTS: Survey of Genotyping Unit

Genotyping Applications



Application Trends

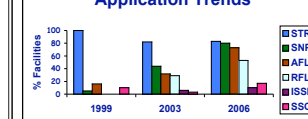


Figure 4: Genotyping Applications: Biomarkers such as microsatellites (STR) and single nucleotide polymorphisms (SNP) are used for linkage and association studies (link), transgene analysis (tg), loss of heterogeneity studies (LOH) and to genotype mixed cell samples (forensic). FLP: fragment length polymorphism; Q (quantitative). **Application Trends:** Data gathered in previous surveys (1999 and 2003) is displayed side by side with the 2006 survey data.

Platform Trends

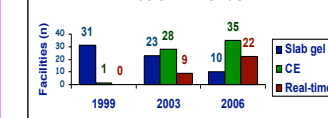


Figure 5: Evolution of the core lab platforms from 1999 to 2006. Slab Gel, CE (capillary electrophoresis) and Real time are three platforms displayed here to illustrate changes that are either manufacturer-driven (retirement of slab gel) or science-driven (Real time/SNP explosion of the post genomic era).

Figure 6: Methods used in core labs: Participants were asked to list the instrument of choice for specific genotyping applications (microsatellite, SNP, Q-PCR, Heteroduplex and RFLP). CE and real time PCR are the major methods of investigation. Alternative approaches include arrayed technologies, pyrosequencing and DHPLC.

