



JOHNS HOPKINS
M E D I C I N E

Aging and DNA methylation.

Delphine Fradin



JOHNS HOPKINS
M E D I C I N E

Centers of Excellence in Genomic Science

Seventh Annual Grantee Meeting

Intra-individual changes over time in DNA methylation.

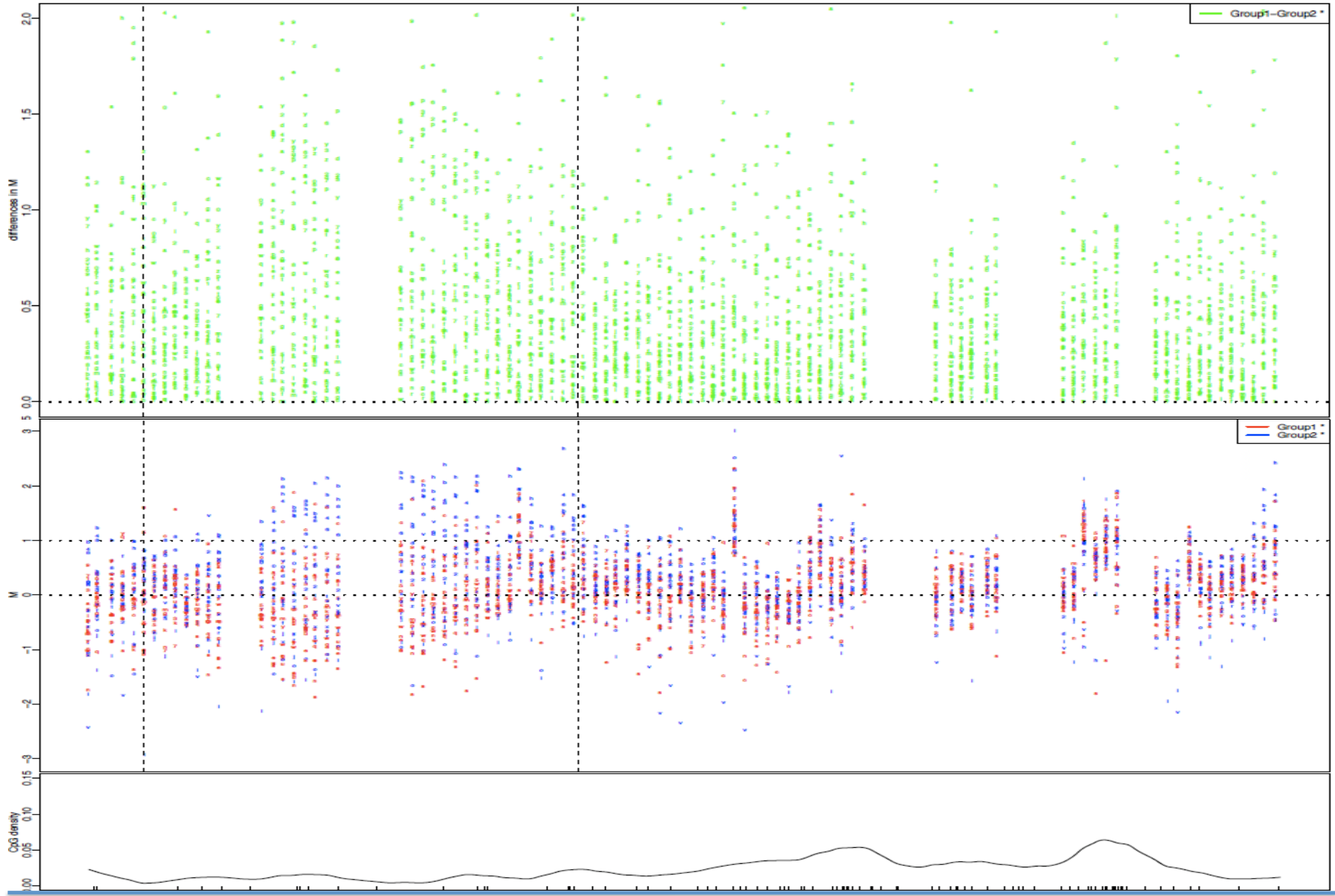
- **AIM: Are there measurable changes in methylation patterns within patient across 15 year time span?**
- Icelandic Heart Association Cohort: AGES-Reykjavik cohort was designed to examine risk factors, including genetic susceptibility and gene/environment interaction, in relation to disease and disability in older age.
 - ✓ 638 participants have DNA samples from 2 visits spanning 15 years
 - ✓ We randomly chose 100 persons among them.

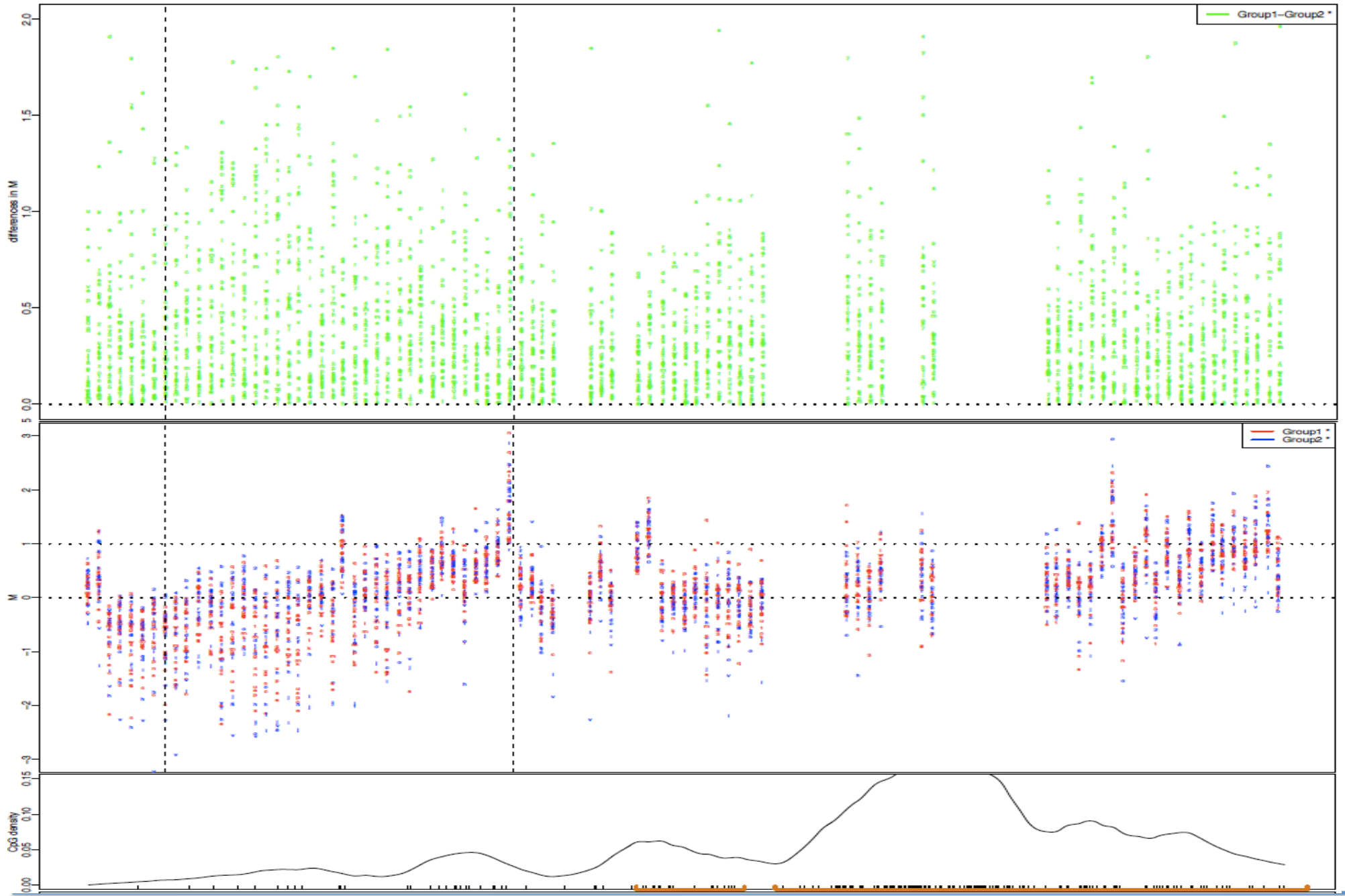
	Dates of examination	Gender	No. of participants in each subcohort						No. of participants examined in each stage
			B	C	A	D	E	F	
Total Reykjavik Study sample (<i>n</i> = 30,795)		Men	2,954	2,743	2,756	2,283	2,106	2,081	
		Women	3,101	2,990	2,936	2,429	2,191	2,225	
Stage of the Reykjavik Study									
VI	1991–1994	Men	664					169	833
	1994–1996	Women	943					267	1,210
AGES–Reykjavik‡	2002–2004	Men	344	320	305	2	5	0	976
	2002–2004	Women	467	414	426	7	10	0	1,324

Harris et al. American Journal of Epidemiology, 2007

Aging - Differential Methylation Regions

- **100 aging patients from IHA:**
 - ✓ 20% men / 80% women
 - ✓ Mean age: 83.4 years a time 2
- We did CHARM on Time 1 and Tim2 for each patient
- **7912** aging-DMRs with a FDR<0.05 (1000 permutations)
 - ✓ The median size of aging-DMR is 713bp
 - ✓ 8% located on promoter, 41% on coding sequence (exon, intron, 5'UTR, 3'UTR)
 - ✓ 33% located on islands and 42% on shores





Aging-DMRs screening

Aging Pathways:

- The p53 pathway: 37% of the gene implicated p53 pathways (from KEGG pathway) present methylation changes over time in our cohort.
- The insulin signaling pathway: 33% of the gene implicated in the insulin signaling pathways
- The calcium signaling pathway: 37% of the gene implicated in the calcium signaling pathways

Adult diseases:

- Cancer: pancreatic cancer 17 genes, prostate cancer 28 genes, colorectal cancer 22 genes, endometrial cancer 17 genes, breast cancer 2 genes...
- Neurodegenerative diseases: Parkinson's disease 5 genes, Alzheimer's disease 9 genes
- Type 2 Diabetes: 20 genes

Progeroid syndromes: 2 genes

Others: Telomere maintenance: 2 genes, Apoptosis 20 genes, Cell cycle 22 genes, Oxidative phosphorylation 23 genes

Conclusion: Epigenetic is an important area in aging biology and may be able to explain many of the phenotypic changes related to the aging process.