

Motif and Population Genetics

Harnessing the Revolution in Genetics

Who is Motif?

Motif BioSciences Inc. is a biotechnology company applying a unique combination of scientific skills and population genetics capabilities to uncover the genetic basis of diseases and drug response.

Overview of Motif's Genomics Approach

- Motif's process begins with the careful selection of a **population** in which the **disease** studied is likely to be more tractable
- Expert **collaborators** and **partners**, often local, are identified for all logistical aspects of the study (e.g., patients and genomics work)
- Motif experts use state-of-the-art statistical methods to **analyze** all data generated

Motif's unique skills

- Population genetics
- Pharmacogenomics
- Statistical genetics
- Bioinformatics

Founder Populations

- Modern groups descended from few individuals
- Settled and remained in one area

GeneMotifs™
Gene patterns associated with susceptibility or resistance to disease, or efficacy / safety profile of drugs

Disease stratification:
drug response and potential risk of adverse events

Pathways for drug discovery:
genetically validated, knowledge of pathway, potential targets for intervention

Motif – A World Class Team

Management Team

Richard C.E. Morgan: Chairman, Co-founder & Director, Celgene (cap value: \$23 bn)

Zaki Hosny: CEO and Deputy Chairman, 35 years at Merck & Co.

Dr. Faisal H. Al-Refaei, MbChB: Regional Director (Middle East)

Scientific Team

Kevin Arnold, PhD: Executive Director Genomics and Operations

Joelle van der Walt, PhD: Project Coordinator Molecular Genetics

Manish Pungliya, MSc: Bioinformatics and Statistical Analysis

Scientific Advisory Board

Jay Tischfield, PhD, Rutgers University

Tara Matise, PhD, Rutgers University

Linda Brzustowicz, PhD, Rutgers University

John Rice, PhD, Washington University

Morris Birnbaum, MD, PhD, University of Pennsylvania

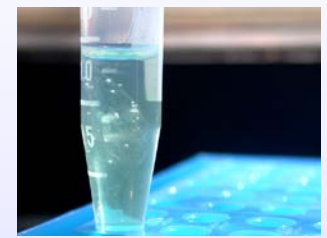
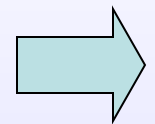
Howard Edenburg, PhD, Indiana University

Raymond White, PhD, University of California, San Francisco

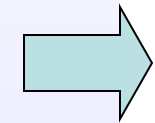
The general process...



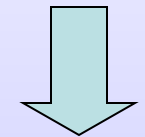
Individuals



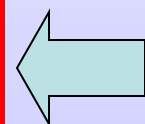
DNA



Genotyping

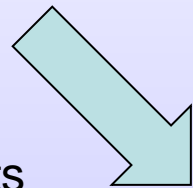


Genotypic results



**Motif:
Motifinder™
GeneMotifs**

Clinical
measurements



Motif's Research Focus: Middle Eastern Populations



- Founder populations.
- High level of consanguinity.
- Rare and common diseases are prevalent.
- Large families available for study.

Example: Partnership with Imperial College

- PI is **Prof. Philippe Froguel**, a world leader in genetics of **Type 2 Diabetes**.
- Genome-wide Association Analysis (**GWA**) on established cohort of **Moroccan** subjects with Type 2 diabetes & Hypertension, Obesity & Dyslipidemia.
- Genotyping on Illumina **1Million SNP chip** at Froguel lab in Lille, France.
- **Data analysis** by Motif using proprietary methodology.
- Imperial owns IP. World-wide **commercial rights** licensed to Motif.

GWA Results (493 Subjects)

Initial

- T2D: 299 Novel Genes identified
- HT: 239 Novel Genes identified
- BMI: 344 Novel Genes identified
- Dyslip: >600 Novel Genes identified

Robust

- T2D: 6-42
- HT: 12-36
- BMI: 3-19
- Dyslip: 4-58

37 of these robustly associated regions were advanced to a replication study of up to 1454 additional subjects

Replication Results (up to 1454 additional subjects)

	<u>A</u>	<u>B</u>	<u>C</u>
➤ T2D:	9	7	2
➤ HT:	17	9	4
➤ BMI:	3	4	0
➤ Dyslip:	2	9	1

A: Regions Advanced

B: Some Replication

C: Strong Replication (multiple analyses, SNPs, and low p-values)



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