

INFOHaemFH™ Chip

A Novel, DNA Microarray Biochip for Screening, Diagnosis and Prognosis of Familial Hypercholesterolemia



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INTRODUCTION

Familial Hypercholesterolemia (FH) is characterized by high LDL (bad) cholesterol levels, leading to excess deposition of cholesterol in tissues and premature heart disease. FH is one of the most common inherited disorders caused by mutations in the LDL-receptor (LDLR) or Apolipoprotein B (APOB) genes. More recently, defects encoding a member of the Proprotein Convertase family, PCSK9 was discovered in patients with FH. The genetic basis to FH is complex and remains poorly understood. Currently, there are no diagnostics kit for making a definite diagnosis of FH, which is indispensable for appropriate disease management.

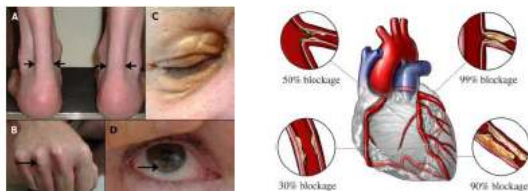


Fig:1: A,B:Tendon Xanthomas C:Xanthelasma D:Arcus cornealis

Fig:2: Cholesterol deposition in Coronaries leading to blockage & heart attacks.

In Malaysian context with present population of ~25 million with a ratio of 1:500 for FH will result in approximately 52,000 people with the disease.

Global healthcare cost is skyrocketing with the United States in almost crisis stage. The Ministry of Health Malaysia has made it clear in their National Healthcare Strategic Plan that the focus has to be in disease prevention through early screening rather than treatment. Heart diseases top the chart both in number of deaths and cost. FH meets the WHO global criteria for disease management.

Present criteria used in diagnosing FH include US MEDPED, Simon Broome's and Dutch Lipid Clinics Network criteria, the latter is most commonly used in clinical practice and hence been used as the basis to establish the new genetic based criteria by the project team. The existing clinical and biochemical criteria are found lacking and inadequate as there is no genetic basis to make a definite and unequivocal diagnosis.

OBJECTIVES

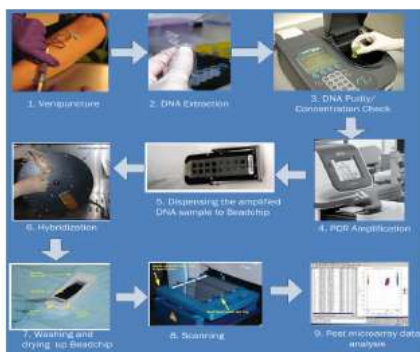
- Determine genotype specific to FH in three major ethnicities of Malaysia
- Design, fabricate, confirm and perform clinical correlation for FH disease management
- Establish and promote a genetic(molecular) based test for FH in clinical practice.

MATERIALS AND METHODS

•Clinical Validation Study: Subjects were recruited from University of Malaya Medical Center (cardiac and endocrine ward and clinic) after obtaining Ethical Committee clearance. Diagnosis was based on Dutch Lipid Clinics Network criteria.

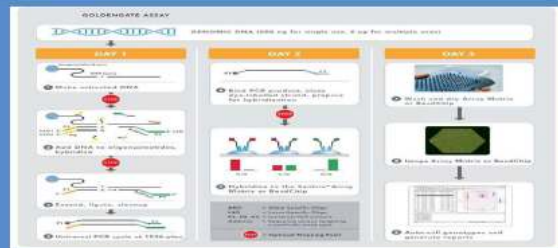


Molecular Analysis was done at Medical Biotechnology Laboratory, Faculty of Medicine, University of Malaya.



Statistical Methods

All the parametric values are expressed as a measure of mean standard deviation (SD). Statistical significance are inferred at a value of $p < 0.05$. Gender, ethnicity, exercise habits, cigarette smoking status, alcohol drinking status are analyzed as binary variables.



ADVANTAGES

- INFOHaemFH™ Chip enables clinicians to make definite diagnosis of Familial Hypercholesterolemia disease by automating & detecting the genes responsible
- It has the ability to determine the type and dosage of drug treatment upon diagnosis
- In clinically healthy persons, the chip can be routinely used to screen and determine possible occurrence of clinically relevant complications of FH.

NOVELTY

- First in world for screening, diagnosis, prognosis and pharmacogenomics in a single chip
- Biological probes designed to meet genetic variation amongst different ethnicities with a special focus on the three major ethnic groups of Malaysia
- Multifold higher in biological probe density in comparison to the nearest and only commercially available chip
- An automated digital environment for management of clinical and molecular data through www.infohaem.com, a portal for generation of Clinico-Molecular Report (CMR).

CONCLUSION

- Our research has successfully identified the genetic and molecular basis of FH in Malaysian ethnic groups
- We were able to design fabricate and validate the chip for FH incorporating local data will serve as an essential, powerful tool that empowers the clinicians (Cardiologists, Endocrinologists) to screen, diagnose and treat FH Patients. The high density biological probes met the challenge of a multi ethnic population as in Malaysia
- INFOHaemFH™ chip will serve as an aid for management of FH by using pharmacogenomics to personalize medicine and to achieve reduction of complications and early deaths in high risk individuals
- Screening of Familial Hypercholesterolemia disease brings awareness and serves as health education to general public, therefore creating community realization on the values of therapeutic lifestyle changes.

REFERENCES

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Photo
(Prof. Rosmawati
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