Figure 1

A

Gb3 and lyso-Gb3 accumulation

Myocytes

Intramycocardial vessels

Conduction tissue

Left ventricular hypertrophy

Cell death

Myocardial ischemia

Myocardial fibrosis

Diastolic dysfunction

Systolic dysfunction

Arrhythmias

Conduction disturbances

B

Genetic defect

Ion channels dysfunction

Degraded proteins

Oxidized proteins

Gb3 - LysoGb3

Apoptosis

Impaired energy production

Impairment of Autophagy

Sarcomere Hypertrophy and dysfunction

Inflammation

Antigen Presenting Cell

INKT

TLR4

cd1d
Figure 2

Established Fabry disease diagnosis

CLINICAL MANIFESTATIONS
- Hypothesis
- Intolerance
- Neurogenic pain
- Gastrointestinal symptoms
- Basal artery dolichoectasia
- Hearing loss
- Renal failure
- Unexplained arrhythmias
- Chest pain

CARCIAL IMAGING
- Concentric LVH
- Hypertrophy of Papillary muscles
- GLS reduction
- Thickening of mitral and aortic valves
- Inferolateral basal LGE
- RVH with normal function
- Inferolateral LGE
- Reduced LV ejection fraction
- Left atrial enlargement
- Left ventricular hypertrophy
- LVH
- LV thrombus
- RVH
- Right atrial enlargement
- Microalbuminuria
- Proteinuria
- Elevated NT-proBNP
- Decreased high-sensitivity Troponin
- Increased plasma LysoGb3
- Reduced eGFR

LABORATORY FINDINGS
- Bradycardia
- Atrioventricular blocks
- Short PQ interval
- Reduced P wave duration
- High QRS voltages
- Negative T waves
- Bradycardia incompetence

ECG
Figure 6

In vivo gene therapy

Ex vivo gene therapy

Modified vector injected into the patient
Modified cells injected back into the patient

Genetic defect

Chaperone therapy

Enzyme replacement therapy

Substrate reduction therapy

Therapeutic gene
Empty vector
Stem cells
Therapeutic gene

M6P receptor
Anti-ERT antibodies

Gb3
Lysoosomes

Correctly folded α-Gal A
Abnormal α-Gal A

Mildly folded α-Gal A

Inhibitor