

# How Much Practice/Knowledge in Basic Science Should Be Included in a Clinical EP Training Program?

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Cardiac Cellular  
Electrophysiology

ESC Working Group



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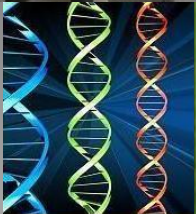
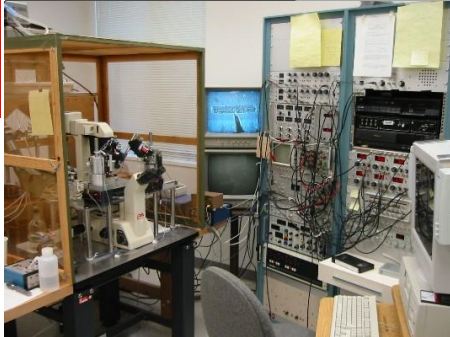
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## Short Answer:

This Depends on the Type of  
Electrophysiologist We Wish to Train

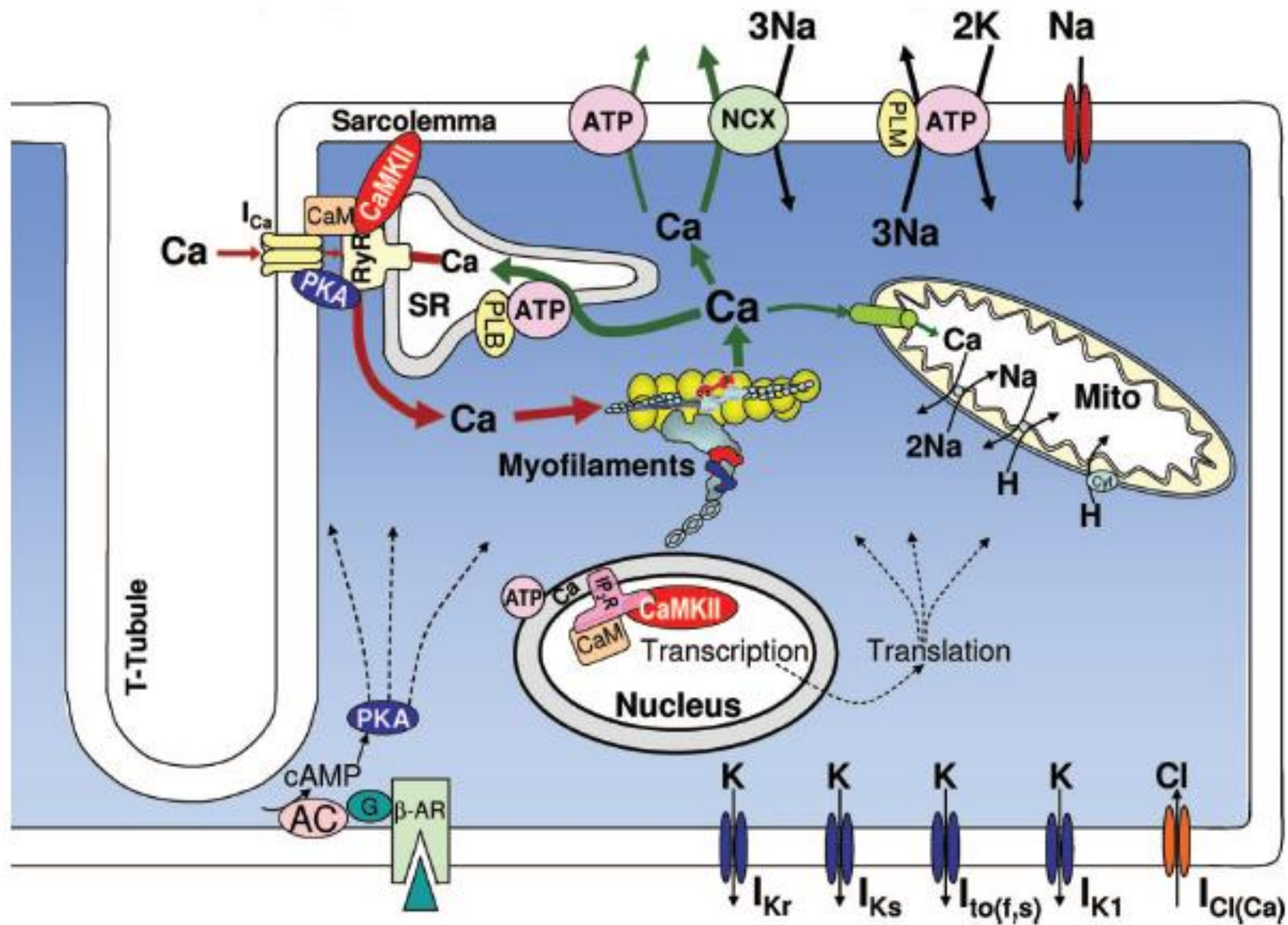
# Basic Cardiac EP and Clinical Cardiac EP:

## Diverging Paths?



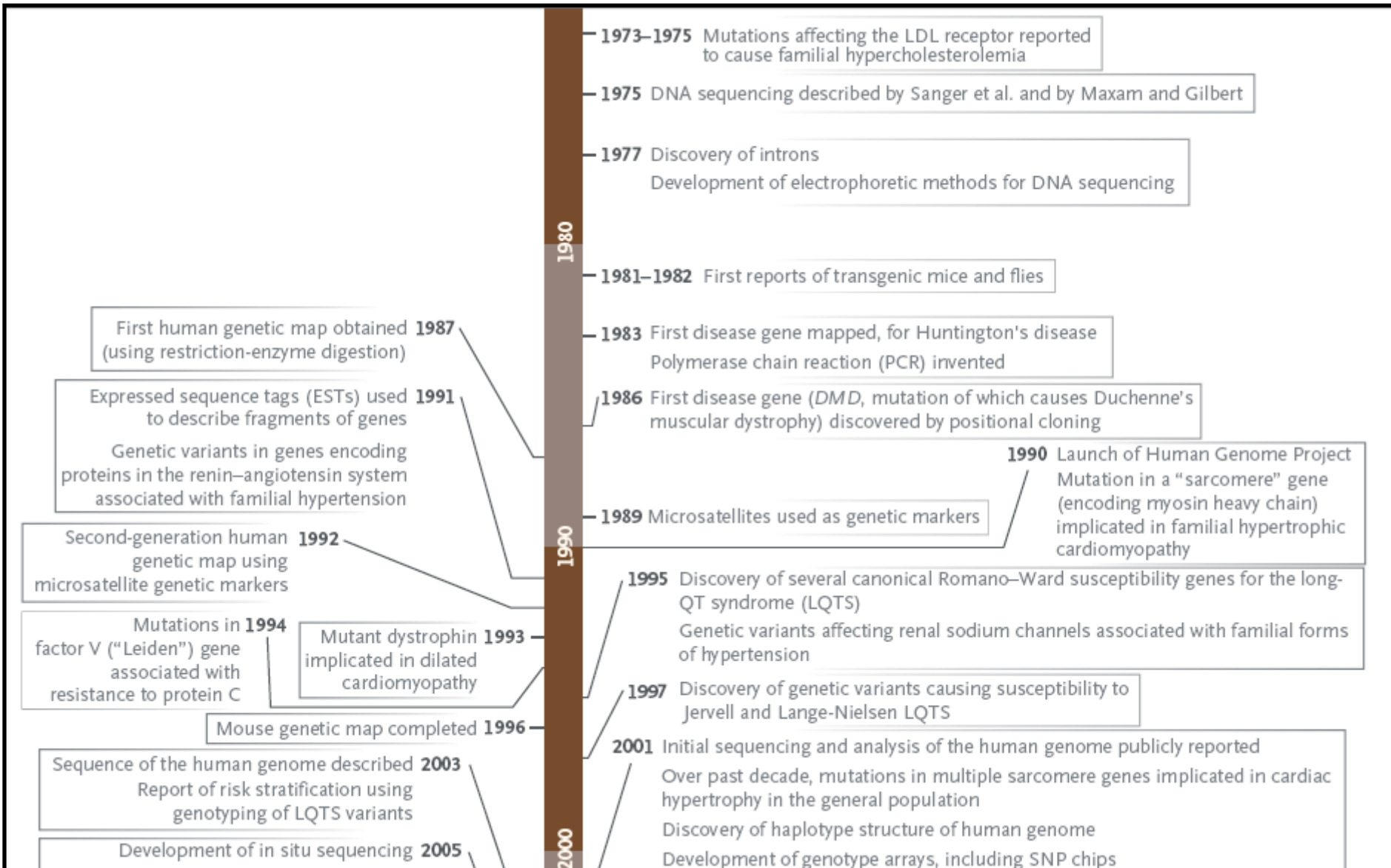
# Aspects of Basic Cardiac EP Relevant for the Clinical Electrophysiologist

- Mechanisms of cardiac impulse formation and impulse conduction
- Mechanisms of **abnormal** impulse formation and impulse conduction
- Calcium handling underlying contraction and other cell functions
- Molecular basis of cardiac electricity
- Ion-channel (related) mutations and their impact on arrhythmogenesis
- **Genetics** of cardiac arrhythmias
- Electropharmacology and antiarrhythmic drugs
- Altered cardiac activation and repolarization in biventricular pacing
- **Computational** (electro)biology of the heart

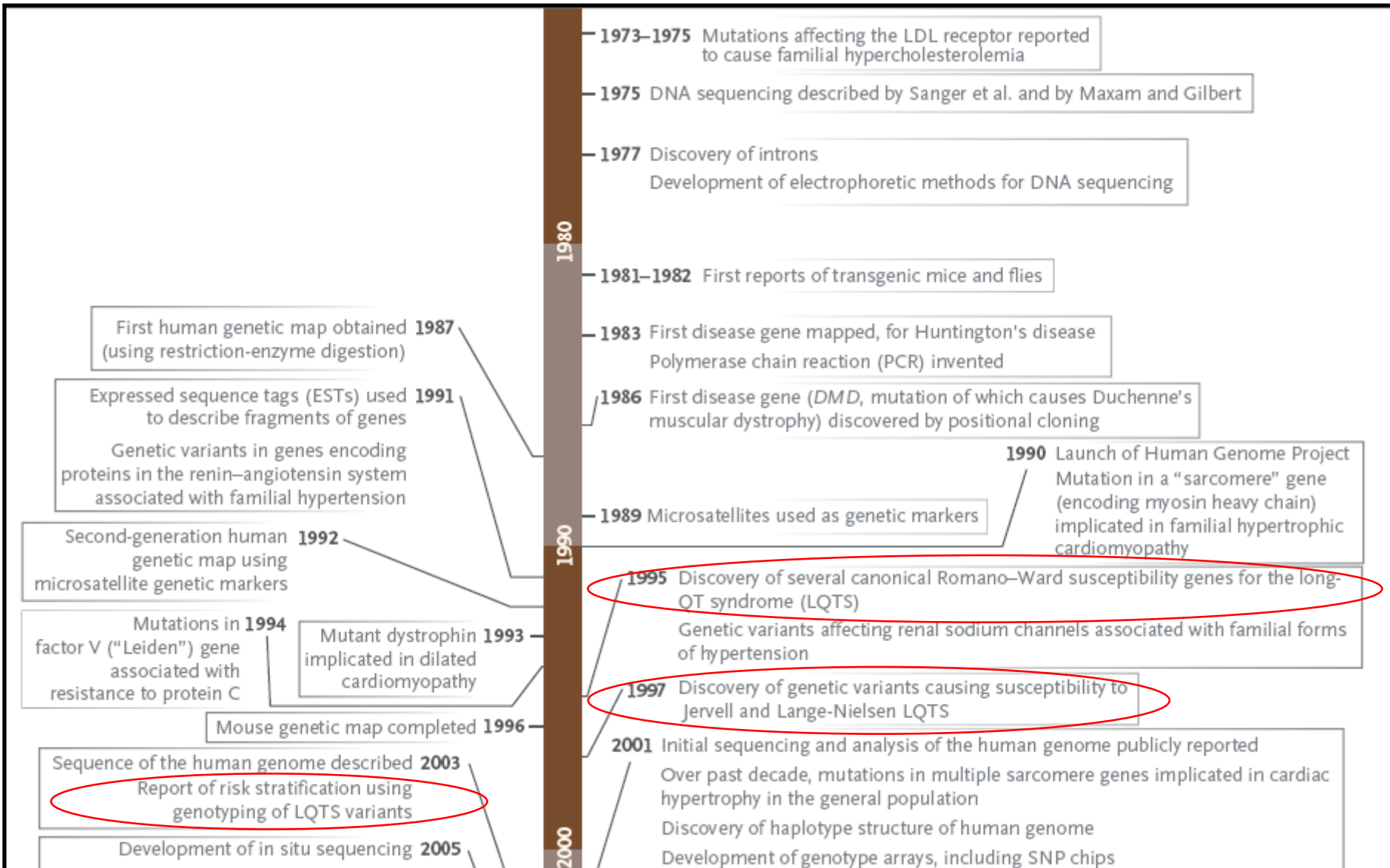




# Timeline of Genetic and Genomic Research in CV Medicine



# Timeline of Genetic and Genomic Research in CV Medicine



Mutations in genes affecting glycogen-storage disease genes shown to cause hypertrophic cardiomyopathy

Detailed map of single-nucleotide variants reported by the International HapMap Project

First report of a gene associated with a cardiovascular trait using GWAS: *NOS1AP* associated with prolonged QT interval

Variants in genes encoding sarcomere proteins and affecting metabolism implicated in cardiac hypertrophy

Mutations in *PCSK9* implicated in lower levels of LDL and lower risk of coronary heart disease

NHLBI begins whole-exome and whole-genome sequencing of the Framingham Heart Study and other cohorts for studying cardiovascular disease.

GWAS implicate genetic variants in early-onset myocardial infarction, QT-interval prolongation, blood pressure and hypertension, echocardiographic measures of cardiac structure, and blood-cell traits.

Exome sequencing identifies mutations in *SLC26A3* for renal salt wasting in Bartter's syndrome.

Large GWAS yields >30 gene loci associated with clinical coronary artery disease.

Large GWAS reports >30 gene loci associated with blood pressure and hypertension.

GWAS also yield variants in *MYH6* associated with sick sinus syndrome and variants associated with dilated cardiomyopathy and carotid intima-media thickness.

2010

2007 Reports of *TCF7L2* and multiple other novel gene loci associated with type 1 and type 2 diabetes mellitus using GWAS

GWAS uncover variants in *FTO* associated with body-mass index and obesity.

Two reports of SNPs at 9p21 associated with myocardial infarction and related forms of coronary artery disease (revealed by GWAS)

Wellcome Trust Case Control Consortium reports associations using GWAS of gene variants with seven conditions including type 1 and type 2 diabetes mellitus and coronary artery disease.

GWAS reveals association between gene variants on chromosome 4q25 and atrial fibrillation.

Phenotype and genotype GWAS data, including those from the Framingham Heart Study, made available in the NIH Database of Genotype and Phenotype (dbGaP)

Phenotype and genotype GWAS data made available in the NIH dbGaP for the MultiEthnic Study of Atherosclerosis and the Women's Health Initiative

2008 Reports of multiple gene loci associated with lipid traits and with body-mass index using GWAS

Reports of loci associated with intracranial aneurysm

Reports of cardiovascular pharmacogenetic effects (prolonged QT interval, increased warfarin maintenance dose, statin-induced myopathy) using GWAS

2010 Large GWAS for CVD risk factors report total of 95 gene loci associated with lipid traits, >30 gene loci associated with type 2 diabetes mellitus, >30 gene loci associated with body-mass index and obesity, and hundreds of variants associated with height

GWAS uncover gene loci associated with cigarette-smoking behavior, sudden cardiac death and ventricular fibrillation, thrombosis factors and platelet function, and ECG interval (RR, PR, QRS).

Variants in 9p21 are found to be associated with abdominal aortic aneurysm.

Exome sequencing identifies *ANGPTL3* mutations in familial combined hypolipidemia.

Whole-genome sequencing identifies *ABCG5* mutations in severe hypercholesterolemia.

Initial report of genomewide sequencing of multiple persons in the 1000 Genomes project





Heart Rhythm Society<sup>SM</sup>  
Restoring the Rhythm of Life

## Translational Electrophysiology (TE) Session Information

**May 10, 2012**

**8:00AM - 9:30AM**

### **Translational Electrophysiology**



[Translational Electrophysiology: How to Become an EP Physician-Scientist](#)

259B

**10:30AM - 12:00PM**

### **Translational Electrophysiology**



[Translational Electrophysiology: How to Develop New Ideas into Products and Therapies](#)

259B

**4:30PM - 6:00PM**

### **Translational Electrophysiology**



[Translational Electrophysiology: Modeling Arrhythmic Disorders in Patient-Derived iPS Cells](#)

259B

**May 11, 2012**

**8:00AM - 9:30AM**

### **Translational Electrophysiology**



[Translational Electrophysiology: The Changing Face of ARVC](#)

259B

**10:30AM - 12:00PM**

### **Translational Electrophysiology**



[Translational Electrophysiology: Update on VF and Defibrillation](#)

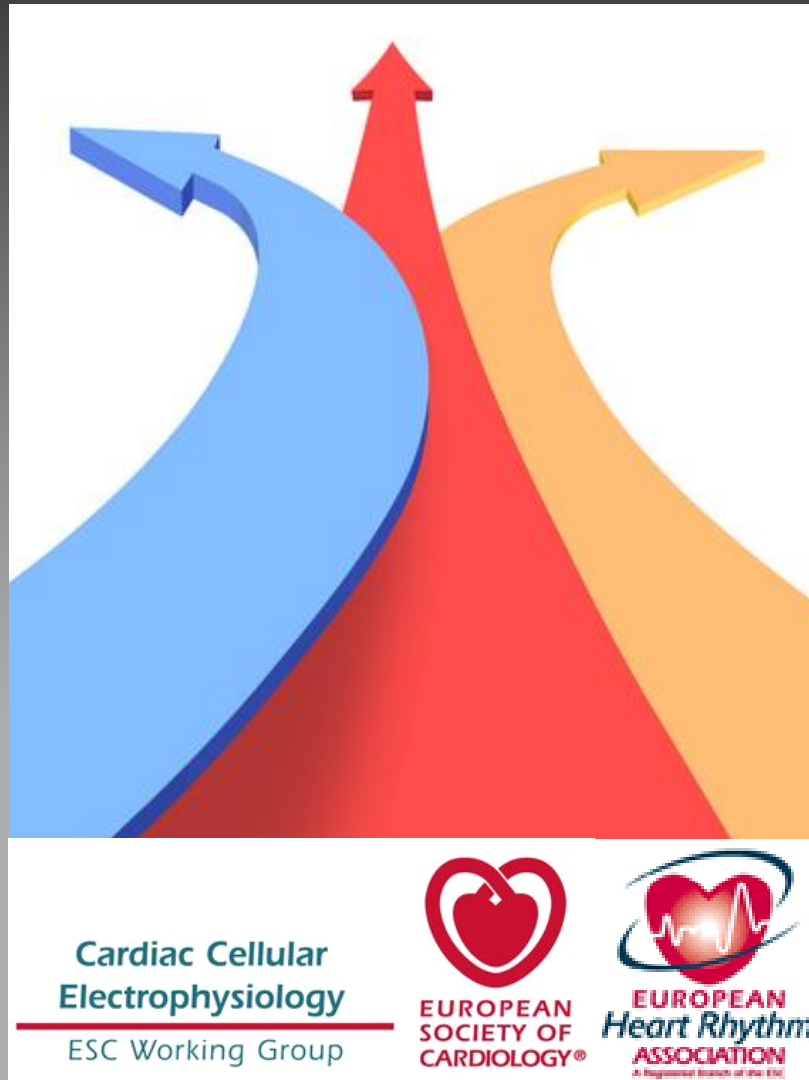
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# Basic Cardiac EP and Clinical Cardiac EP:

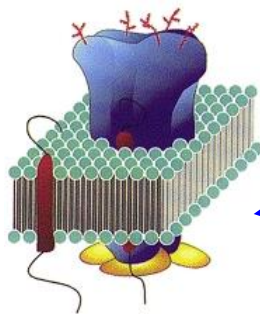
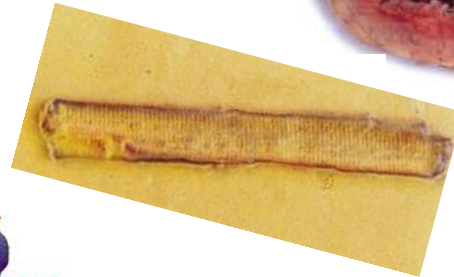
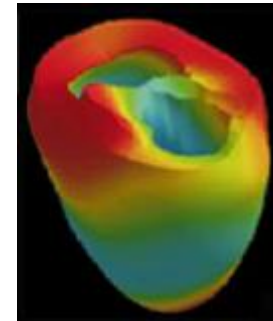
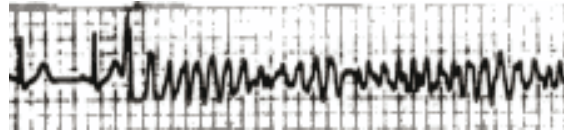
## Diverging Paths?



# EWGCCE/EHRA Translational EP Curriculum



# Systems-Biology Approach



Experimental lines

Computational integration



Discovering, Practicing,  
Translating, Transforming







Heart Rhythm Society<sup>™</sup>  
Restoring the Rhythm of Life

## Translational Electrophysiology (TE) Session Information

### Chair:

Dan M. Roden, MD. Vanderbilt University School of Medicine, Nashville, TN

### Presentations:

☐ Thursday, May 10, 2012, 8:00 AM - 8:20 AM

[My Journey: Insights On Achieving A Successful Career as an Electrophysiologist and Physician-Scientist in the New England](#)

Christine M. Albert, MD. Brigham and Women's Hospital, Boston, MA

☐ Thursday, May 10, 2012, 8:20 AM - 8:40 AM

[My Journey: Insights On Achieving A Successful Career as an Electrophysiologist and Physician-Scientist in the Mid-Atlantic and Mid-West](#)

J. Kevin Donahue, MD. Case Western Reserve University - MetroHealth Campus, Cleveland, OH

☐ Thursday, May 10, 2012, 8:40 AM - 9:00 AM

[My Journey: Insights On Achieving A Successful Career as an Electrophysiologist and Physician-Scientist on the West Coast](#)

Kalyanam Shivkumar, MD, PHD, FHRS. UCLA Cardiac Arrhythmia Center, Los Angeles, CA

☐ Thursday, May 10, 2012, 9:00 AM - 9:20 AM

[My Journey: Insights On Achieving A Successful Career as an Electrophysiologist and Physician-Scientist in New England and the Mid-West](#)

David S. Rosenbaum, MD, FHRS. MetroHealth Campus, Case Western Reserve University, Cleveland, OH