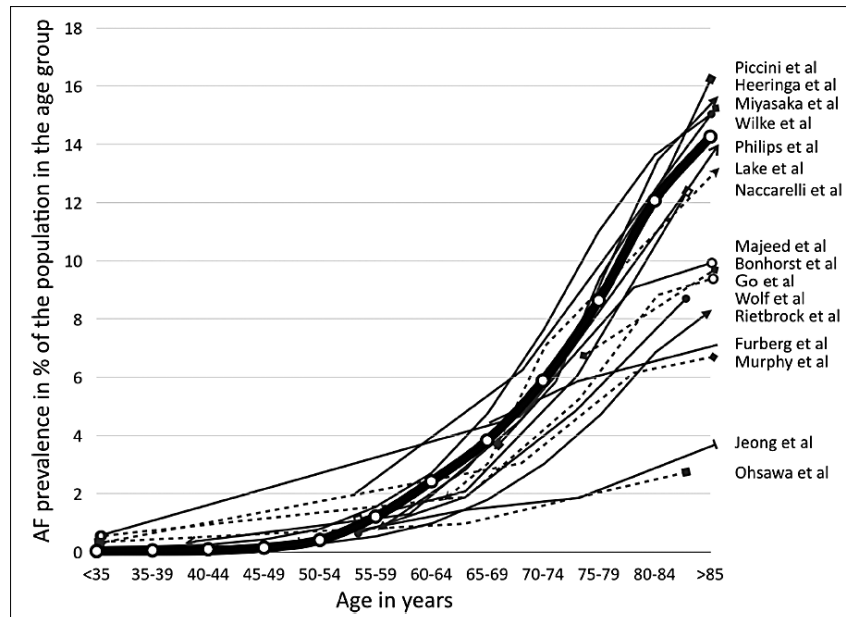


The Scope of Atrial Fibrillation Children to Adults

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Demographics and Atrial Fibrillation

- Atrial Fibrillation (AF) currently affects **1% to 2%** of the general population.
- AF is the most common arrhythmia with an estimated lifetime risk of **22% to 26%**.
- The prevalence of AF is **<0.5%** at 40-50 years.
- Age is arguably the strongest determinant of AF occurrence.



Camm AJ, et al. Guidelines for the management of atrial fibrillation. Europace. 2010;1360–1420.

Andrade J, et al. The Clinical Profile and Pathophysiology of Atrial Fibrillation. Circ Res. 2014;1453-1468.

Clinical Profile of Atrial Fibrillation

- Men are more often affected than women.
- Clinical presentations range from asymptomatic to debilitating reflecting, in part, the heterogeneity in associated comorbidities.
- AF is silent in ≤ 5 to 35% of adult patients.
- The prevalence of asymptomatic AF in children and young adults?

AF Risk Factors in General Population

Risk Factor	Estimated Increased Risk	Comments
Established		
Age	≈2	Per decade
Male sex	1.5	
Hypertension	1.2–1.5	BP >140/90 mm Hg
Valvular heart disease	1.8–3.4	
LV systolic dysfunction	4.5–5.9	
Obesity	1.39–2.35	
Alcohol consumption	1.34–1.46	Heavy alcohol use (≥36 g/d)
Emerging		
Prehypertension	1.28	Systolic BP 130–139 mm Hg vs <120 mm Hg
Increased pulse pressure	1.26	Per 20-mm Hg increment
Obstructive sleep apnea	2.8–5.6	
Physical activity	2.87	Cumulative lifetime practice >1500 h
Diastolic dysfunction	3.33–5.26	
Familial and genetic	1.85	AF in ≥1 parent
Hypertrophic cardiomyopathy	4–6	
Congenital heart disease	N/A	
Potential		
Coronary artery disease	N/A	Data inconclusive
Chronic kidney disease	1.3–3.2	Graded risk
Inflammation	1.47–1.77	Independent predictive value unclear
Pericardial fat	1.28–5.30	Risk related to thickness and volume of pericardial fat
Tobacco use	1.51–2.05	

AF Risk Factors in Children and Adolescents

- ?
- Male predominance: 75% versus 25%
 - Congenital Heart Disease
 - LV systolic dysfunction
 - Hypertrophic Cardiomyopathy
 - Obesity/Alcohol consumption/Pre-HTN
 - Lone AF:
 - Familial AF:
 - WPW Syndrome/SVTs:
 - Inherited Arrhythmogenic Disorders: (LQTS, SQTs, BrS, CPVT)

Andrade J, et al. The Clinical Profile and Pathophysiology of Atrial Fibrillation. Circ Res. 2014;1453-1468.

Congenital Heart Disease and Atrial Fibrillation

- AF is increasing in prevalence in the aging population with CHD. In a series of patients with CHD undergoing cardioversion over a 10-year period, 31% had AF.
- Overall, macroreentrant AT is more frequent than AF. AF surpasses macroreentrant AT as the most prevalent atrial tachyarrhythmia over the age of 55 years.
- AF mechanisms (Pulmonary Veins – Atria)?
- Therapeutic options:
 - Anticoagulation!
 - AARx (Amiodarone)
 - Catheter ablation – PV Isolation (success rate of 60% at 4-years)

Khairy P, et al. PACES/HRS Expert Consensus Statement on the Recognition and Management of Arrhythmias in Adult Congenital Heart Disease. Heart Rhythm 2014;e102–e165.

Philip F, et al. Pulmonary Vein Isolation for the Treatment of Drug-Refractory Atrial Fibrillation in Adults with Congenital Heart Disease. Congenital Heart Dis. 2012;392–399.

Dilated Cardiomyopathy and Atrial Fibrillation

- DCM represents 55% of all cardiomyopathies in children. The incidence is 0.53 cases per 100 000 children, which is one-tenth the incidence of adult DCM.
- Two-thirds of children are thought to have idiopathic disease.
- AF is rare in children and young adults.
- AF mechanisms (Pulmonary Veins – Atria)?
- Therapeutic options:
 - Anticoagulation!
 - AARx (Amiodarone)
 - Catheter ablation?

Bozkurt B, et al. Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies: A Scientific Statement From the American Heart Association. Circulation. 2016;;e579-e646.

Hypertrophic Cardiomyopathy and Atrial Fibrillation

- AF is seldom seen in patients with HCM who are < 30 years of age and becomes more prevalent with age.
- ~ 20-25% of patients develop AF with an annual incidence of 2%.
- AF is an indicator of unfavorable prognosis, including increased risk of HCM-related heart failure, death, and stroke.
- AF mechanisms (Pulmonary Veins – Atria)?
- Therapeutic options:
 - Anticoagulation!
 - AARx (Amiodarone) – Dronedarone/Disopyramide/Ic-agents?
 - Catheter ablation

Gersh BJ, et al. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy: Executive Summary. Circulation. 2011;:2761-2796.

Lone AF

AF in younger adults (age <60 years) with no clinical history or echocardiographic evidence of concomitant cardiovascular or pulmonary conditions or an acute trigger.

Children and Adolescents

- M >> F
- Prevalence ?
- Familial nature ~ 15%
- Natural course: Recurrence ~ 40%
- Co-existing SVTs ~ 10-40%
- Trigger(s): ~ Pulmonary veins
- Genetic in nature: Most likely

Mills LC, et al. Lone Atrial Fibrillation in the Pediatric Population. Canadian Journal of Cardiology. 2013;1227-1233.

Ceresnak SR, et al. Lone Atrial Fibrillation in the Young – Perhaps Not So “Lone”? J Pediatr. 2013;:827-31.

Adults

- M >> F
- Prevalence ~ 5-10%
- Familial nature ~ 30%
- Natural course: Recurrence ~40%
- Co-existing SVTs ~ 5% (All-AF pts)
- Trigger(s): ~ Pulmonary veins
- Genetic in nature:
 - Loss-of-function mutations
 - Gain-of-function mutations

Wyse GD, et al. Lone Atrial Fibrillation. Does it Exist? JACC. 2014;1715-1723.

WPW Syndrome and Atrial Fibrillation

- AF develops in ~ 6-12% of patients.
- AF is rare in infants.
- Spontaneous (75-85%) or AVRT-induced AF (15-25%).
- Accessory pathway(s) ablation decreases the risk of AF by 80 to 90%.
- AF mechanisms (Atria >> Pulmonary Veins)?
- The overall incidence of sudden death in patients with structurally normal heart is 1.1-1.5/1000 patient-years. Sudden death rate is higher in children with structural heart disease:
 - VSD
 - Ebstein's Anomaly
 - Corrected transposition of the great arteries
 - Coarctation of the aorta

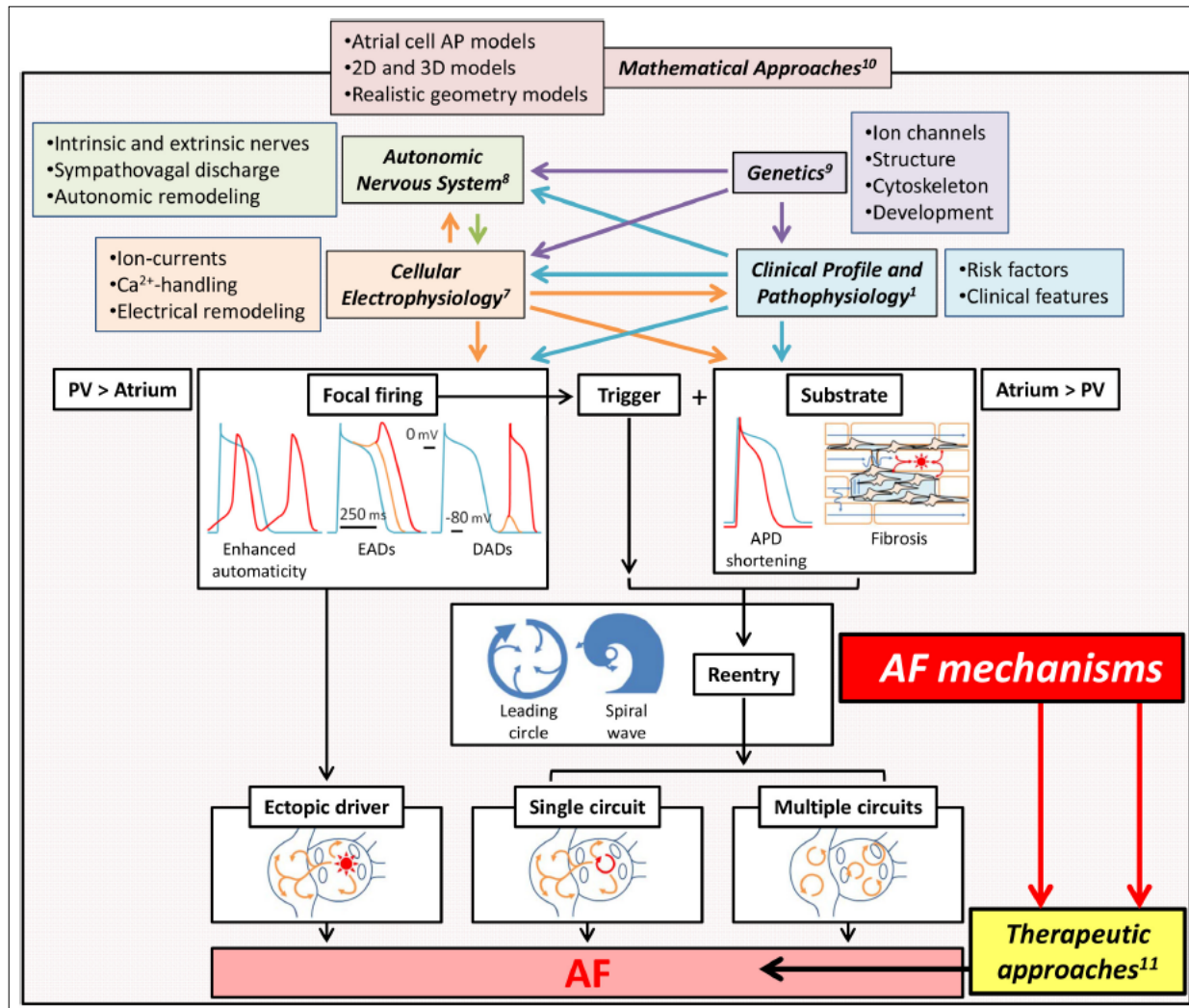
~ 10%

Cain N, et al. Natural History of Wolff-Parkinson-White Syndrome Diagnosed in Childhood. Am J Cardiol. 2013;:961-965.

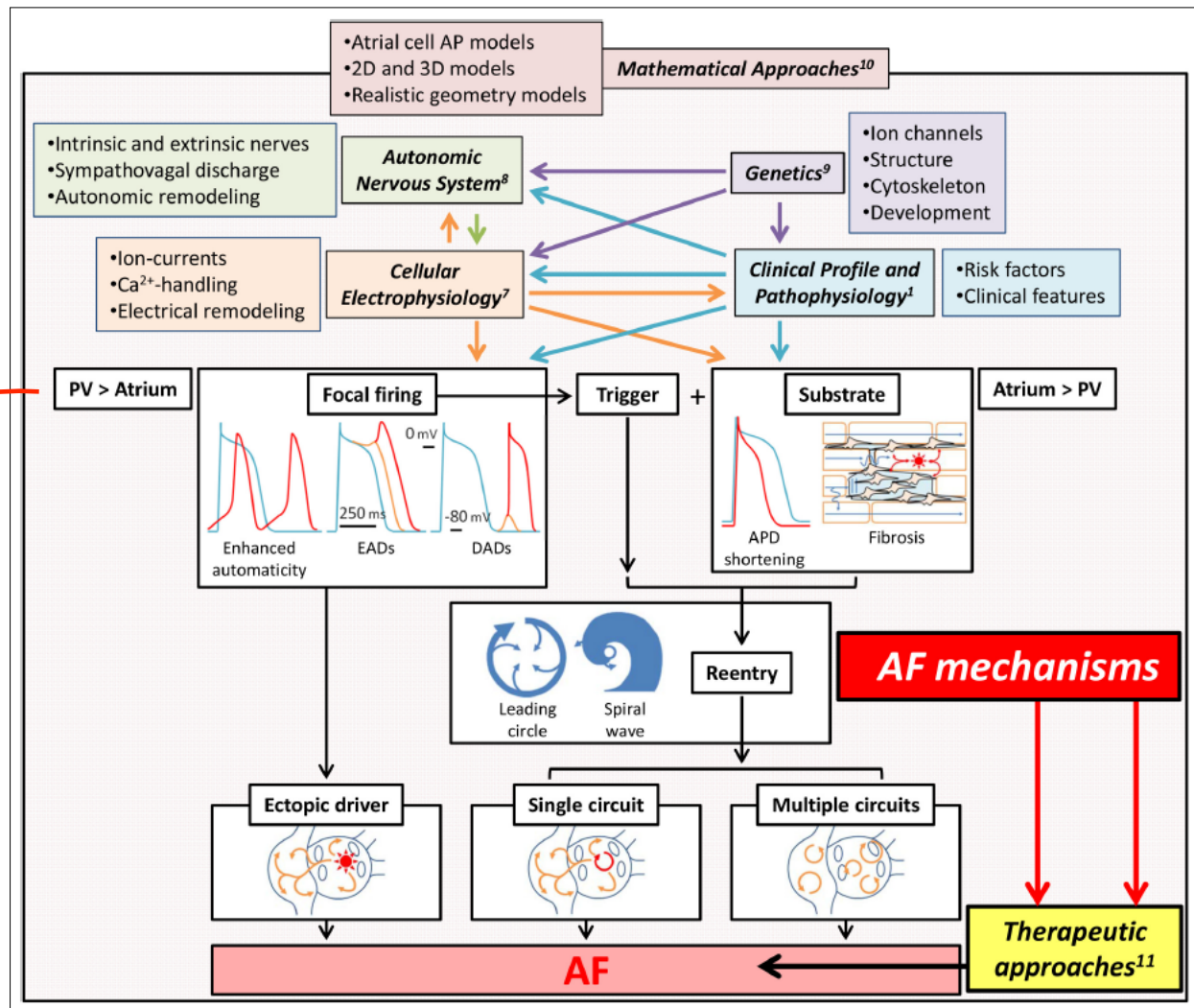
Inherited Arrhythmogenic Disorders and Atrial Fibrillation

- **Long QT syndrome:**
 - Prevalence of AF/AFL – **1.7%** (All patients had type 1 LQTS)
 - Atrial Torsades de Pointes!
- **Short QT syndrome:**
 - Prevalence of AF/AFL – **11 to 16%** -- Frequently Familial
 - More common in type 2 SQTS (KCNQ1)
- **Brugada syndrome:**
 - Prevalence of AF/AFL – **5 to 10%**
 - Pulmonar Veins >> Atria
- **Catecholaminergic Polymorphic VT:**
 - Prevalence of AF/AFL/AT – **22%**
 - Sinus node dysfunction is common – 5 to 20%

Cellular and Molecular Electrophysiology of AF Initiation, Maintenance, and Progression



Nishida K and Nattel S. Atrial Fibrillation Compendium. Historical Context and Detailed Translational Perspective on an Important Clinical Problem. *Circ Res.* 2014;1447-1452.

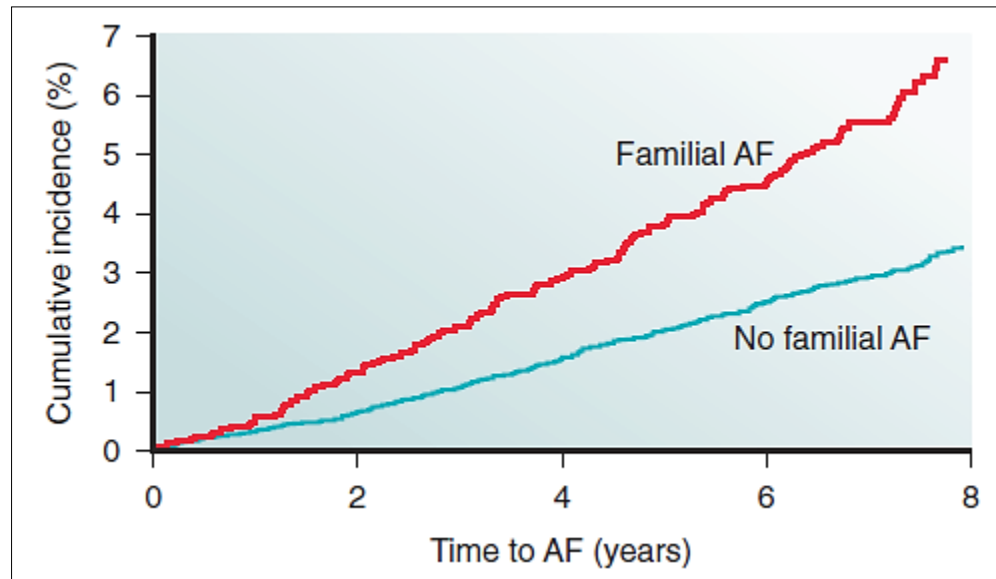


Nanthakumar K, et al. Electrophysiological Findings in Adolescents With Atrial Fibrillation Who Have Structurally Normal Hearts. *Circulation*. 2004;117-123.

Balaji S, et al. Catheter Ablation of Recurrent Lone Atrial Fibrillation in Teenagers with a Structurally Normal Heart. *PACE* 2016;:60–64.

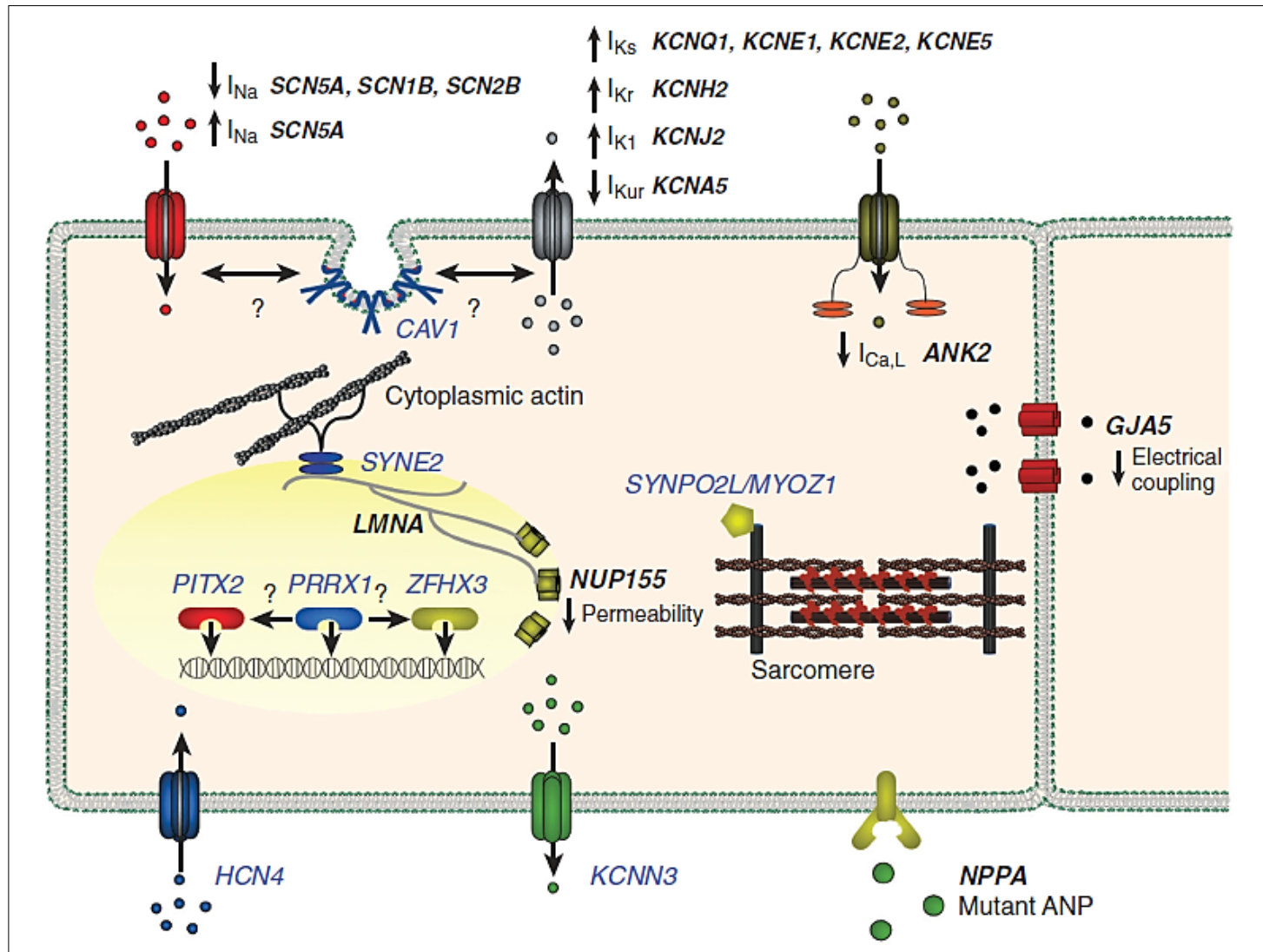
Genetics of Atrial Fibrillation

- In the community-based Framingham Heart Study, 27% of individuals with AF had a first-degree relative with AF confirmed by electrocardiography.
- Familial AF was associated with a 40% increased risk of AF for another family member over a subsequent 8-year period.



- The heritability of AF appears to be greatest among younger individuals and those without structural heart disease.

Lubitz SA, Ellinor PT. Genetics of Atrial Fibrillation. Cardiac Electrophysiology: From Cell to Bedside, Sixth Edition. 2014; 483-488.



Genes Implicated in the Pathogenesis of Atrial Fibrillation

Atrial Fibrillation Therapy

- **Rate Control:**
- **Rhythm Control:**
 - AARx (Amiodarone/Dronedarone/Ic-agents)
 - Catheter Ablation: RF versus Cryoablation in children?
- **Anticoagulation:** Warfarin versus NOACs in children?

CHA₂DS₂VASc

C = Congestive Heart Failure/LVEF↓
 H = Hypertension
 A = Age ≥ 75
 D = Diabetes Mellitus
 S = Stroke/TIA
 V = Vascular Disease
 A = Age 65-74
 Sc = Sex (Female gender)

≥ 1 = Anticoagulation

HAS-BLED

H = Hypertension
 A₂ = Abnormal hepatic/renal functions
 S = Stroke
 B = History of bleeding/anemia
 L = Labile INR
 E = Elderly > 65
 D₂ = Drugs/Alcohol Intake

≥ 3 = High Risk