Cardiac biomarkers: present and the future
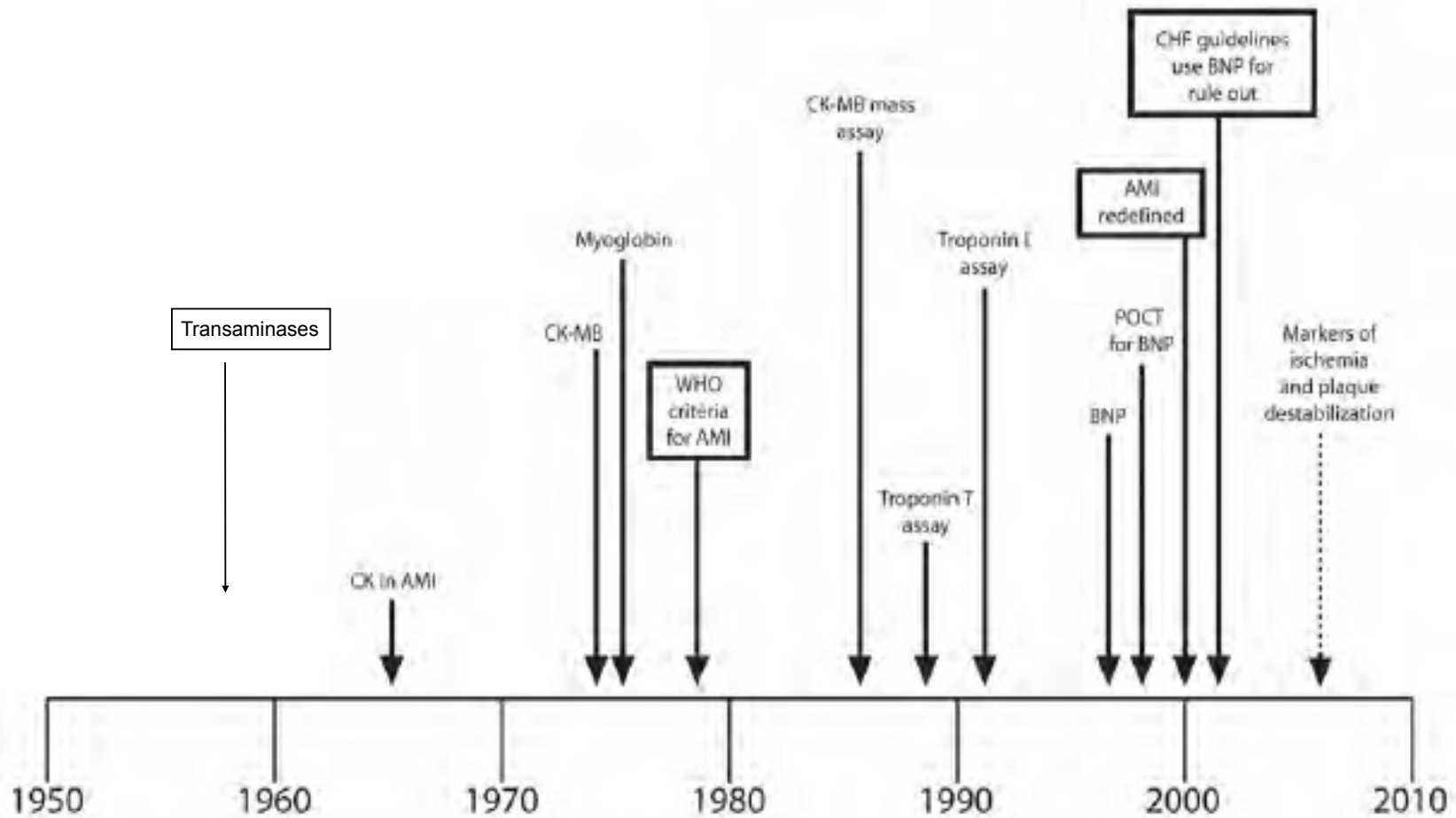
Caroline Le Goff
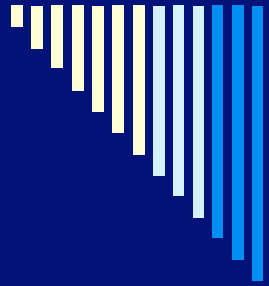**University Hospital of Liège**
June 18th
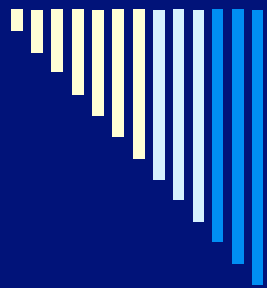**IFCC- Task Force-Young Scientists**

History

Cardiac biomarkers: what we have now!

- Cardiac Necrosis
- Remodeling
- Inflammatory response
- Myocyte Injury/Stress-Myocardial ischemia
- Plaque destabilisation

Cardiac Necrosis and Ischemia biomarkers

| Biomarker	Molecular Weight (kDa)	Initial Elevation in blood	Time to peak	Return to normal	Type of Marker	Comments
H-FABP	15kDa	1-2 hrs	6-8 hrs	24 hrs	Ischemic	Early rise Highly specific
Myoglobin	17kDa	1-3 hrs	5-8 hrs	16-24 hrs	Ischemic	Early rise Highly unspecific
Troponin I (TnI)	22kDa	3-6 hrs	14-18 hrs	5-10 days	Necrotic	Late rise Very Highly specific
Troponin T (TnT)	33kDa	3-6 hrs	10-48 hrs	10-15 days	Necrotic	Late rise Very Highly specific
CK-MB	86kDa	3-8 hrs	9-24 hrs	48-72 hrs	Necrotic	Late rise Relatively specific
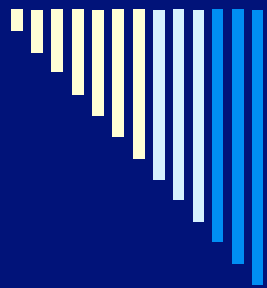
Cardiac Necrosis biomarkers

Troponins I and T

- ☐ The biochemical « gold standard »
- ☐ Specific of AMI
- ☐ I : completely specific for heart
- ☐ T: released small amounts by skeletal muscles
- ☐ Increase with cardiac insufficiency, angina…
- ☐ Elevated levels can persist for weeks; retrospective diagnosis of infraction.
- ☐ CKD
- ☐ New highly sensitive: good or more false positive: is what really necessary?

Ischemia biomarkers

H-FABP (heart-type fatty acid binding protein)
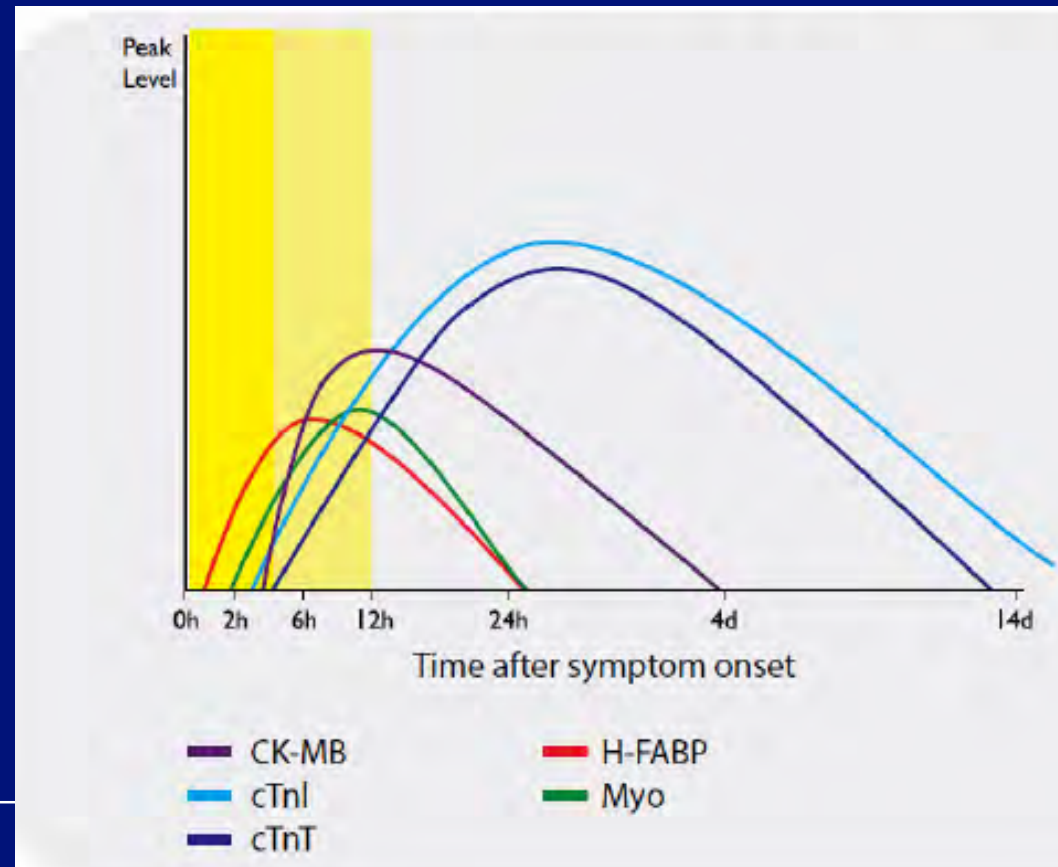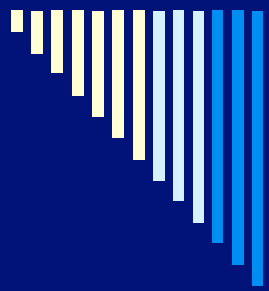
Ischemia biomarkers

H-FABP (heart-type fatty acid binding protein)

- ☐ Early rise marker of ACS (30 min following the onset of an ischemic episode)
- ☐ Marker for re-infarction
- ☐ Combination with Tn☐ improve the diagnostic sensitivity for MI/ACS
- ☐ Not widely use in practice
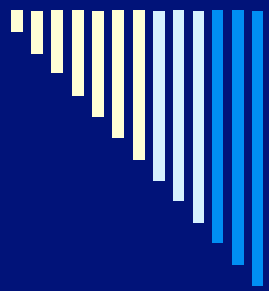
Myocyte injury/Stress

o Natriuretic peptide

o ↪ BNP, NT-proBNP, ANP

o Especially useful in ruling out heart failure as cause of dyspnea given its excellent negative predictive value.

o BNP and NT-proBNP: more specific of cardiac dysfonction➜ clinical interest+++
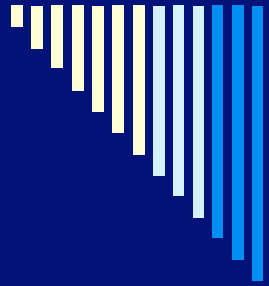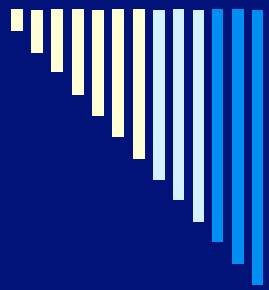
Myocyte Injury/Stress
Copeptin

- *Endogenous stress*
- Elevated after AMI and associated with LV dysfunction and remodeling and clinical HF post-AMI
- In acute and chronic HF$\rightarrow$ elevation of it$\rightarrow$ predicts disease severity and poor outcome
- 99.7% NPV
- May obviate the need of prolonged monitoring and serial blood sampling
- Has been said>to and an additive to BNP
- Best single predictor of mortality in patients with NYHA functional class II and III

Myocyte injury/Stress

GDF 15

- Only detectable in liver and placenta➜ can induced in the heart by MI and pressure overload
- Strong predictor of mortality in some patients
- Similar prognostic as NT=proBNP
- Role to play in diagnosis and risk stratification in HF
- The exact pathophysiological mechanisms of GDF-15 in the cardiovascular system and in acute ST-elevation myocardial infarction (STEMI) are not well defined.
- Not widely use in practice

Remodeling biomarker

*Matrix metalloproteinase (MMP9) :*

- *The main cause of fibrous cap disruption in plaque rupture*
- *Associated with higher mortality rates in HF --> Prognosis in HF*
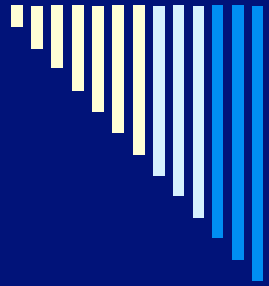
Remodeling biomarker

Galectin 3

- ☐ *Link between inflammation and fibrosis*
- ☐ *Early marker of potential myocyte dysfunction and it may be a marker of early remodeling*
- ☐ *Increased in HF*
- ☐ *Diagnostic role (<NT-proBNP)*
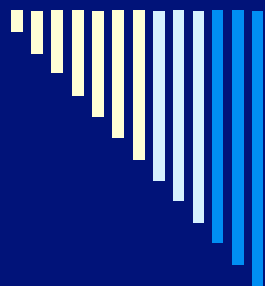- ☐ *Prognosis (>to NT-proBNP in short term)*
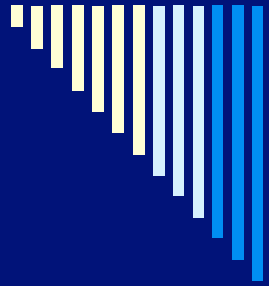
Inflammatory response

Highly sensitive CRP
- Plasma levels can increase rapidly in response to acute inflammation
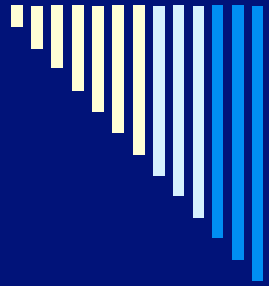- Risk factor or risk marker?

MPO
- Activated leukocytes
- Predicts cardiac risk independently of other markers of inflammation
- IL (1,2,18)

$\rightarrow$ NOT specific

Clinical advantages and disadvantages of more interesting biomarkers

Biomarkers	Advantages	Disadvantages
Troponins HS	Elevated after 8h	Elevated in non-MI cases
	Elevated for 7-10 days	Need 2nd test if 1st too early
	Cardiac specific	Some TNT in skeletal muscle
	Very sensitive	Incomplete understanding of elevation post cardiac and non cardiac surgery
	Stratifies short and long terms risk in AMI	Baseline higher in CRF
	Detects reinfarction	
	Correlates to MI	
Myoglobin	Theoretically rapid detection	Lack of specificity
CRP HS	Marker of inflammation	Not specific
Copeptin	If level low--> rules out MI	Not specific
H-FABP	Early marker of ischaemia	Disappointing in studies
BNP (NT-pro)	Prognistication in AMI	Difficlut to interpret in critical ill
MPO	Elevated in inflammation	Not superior

The dream biomarker: what we wish…

- ☐ **Specificity**
- ☐ **Sensitivity**
- ☐ **Predictibility**
- ☐ **Durability**
- ☐ **Fiability**
- ☐ **Simplicity**
- ☐ **Quickly**
- ☐ **Cost**
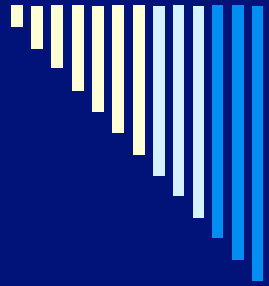
The future….

- Multiple biomarkers approach show a best choice….
- TnThs…
- Metabolomic and proteomic