

VASCULAR PROTEOMICS

AT THE CROSSROAD OF

CHRONIC KIDNEY DISEASE

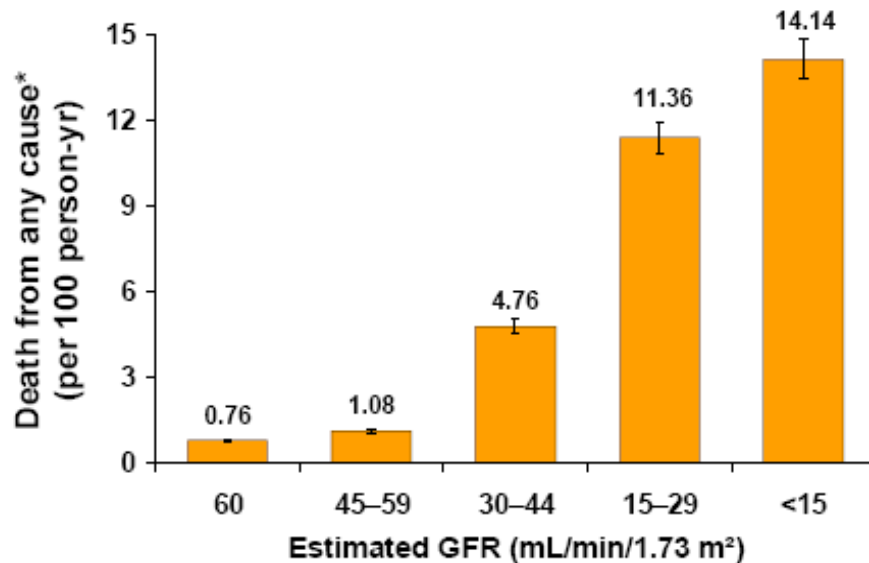
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Chief ,Division of Nephrology and Hypertension
Fundación Jiménez Díaz. MADRID

Nafplio, 29-30 , March, 2009

Independent Effect of CKD on CVD Morbidity / Mortality

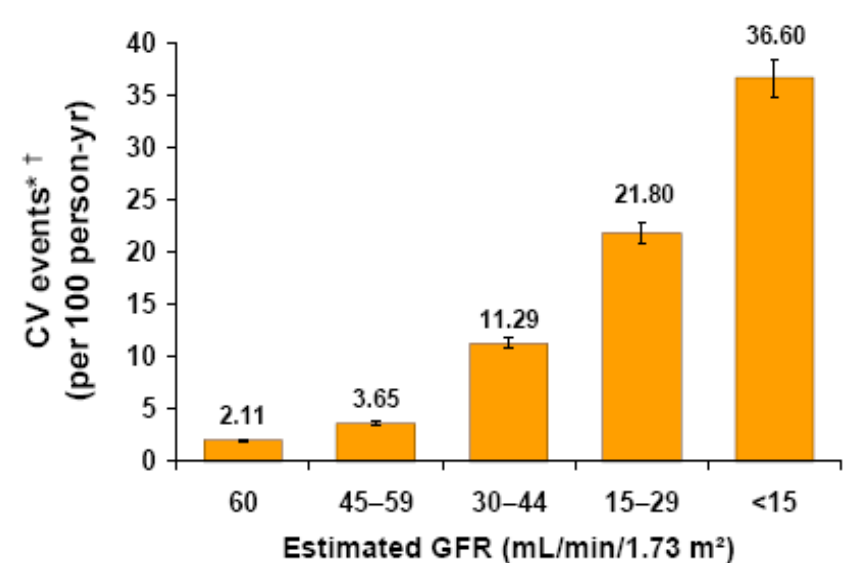
N=1,120,295 adults

Deaths from any cause



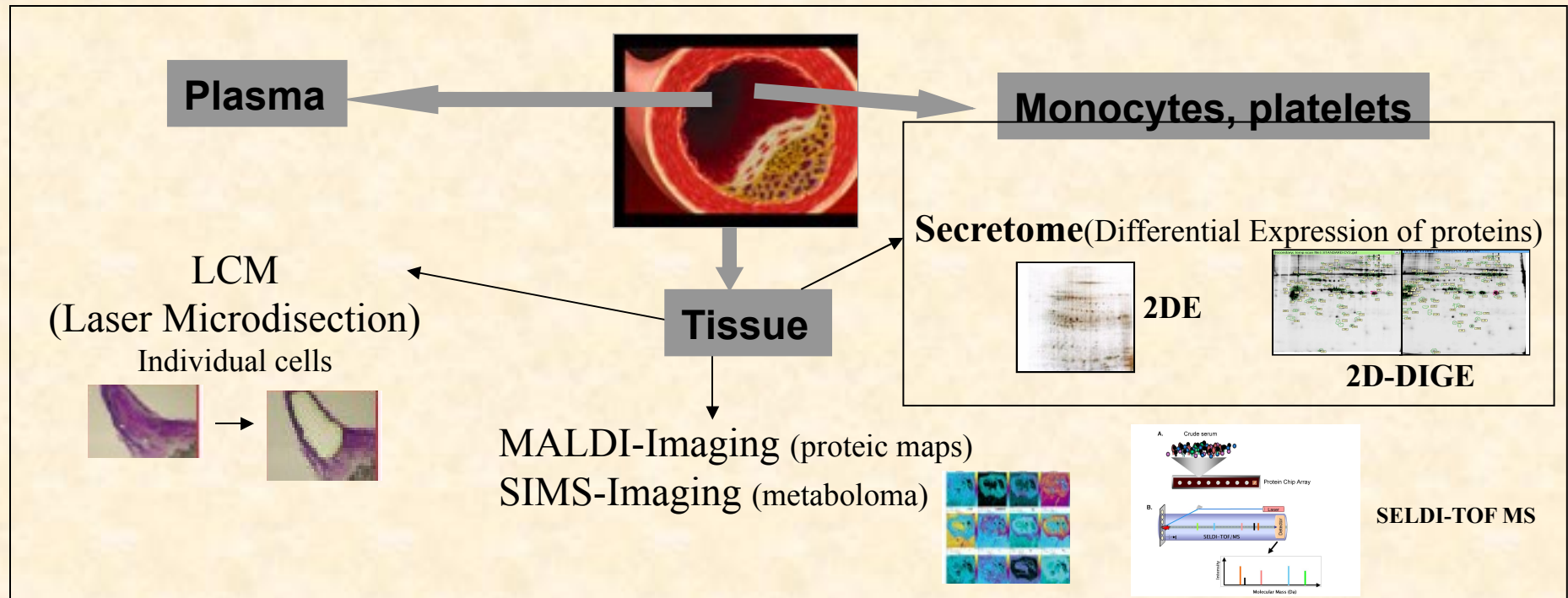
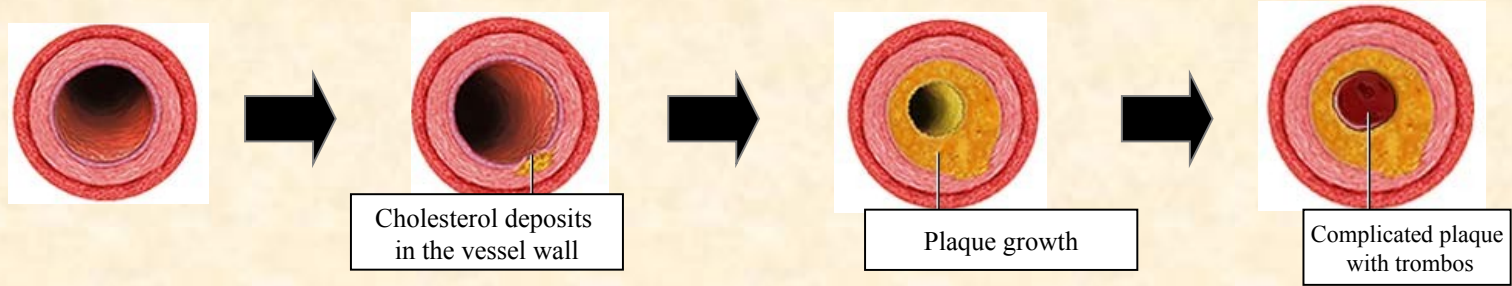
No. of Events	25,803	11,569	7,802	4,408	1,842
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CV events

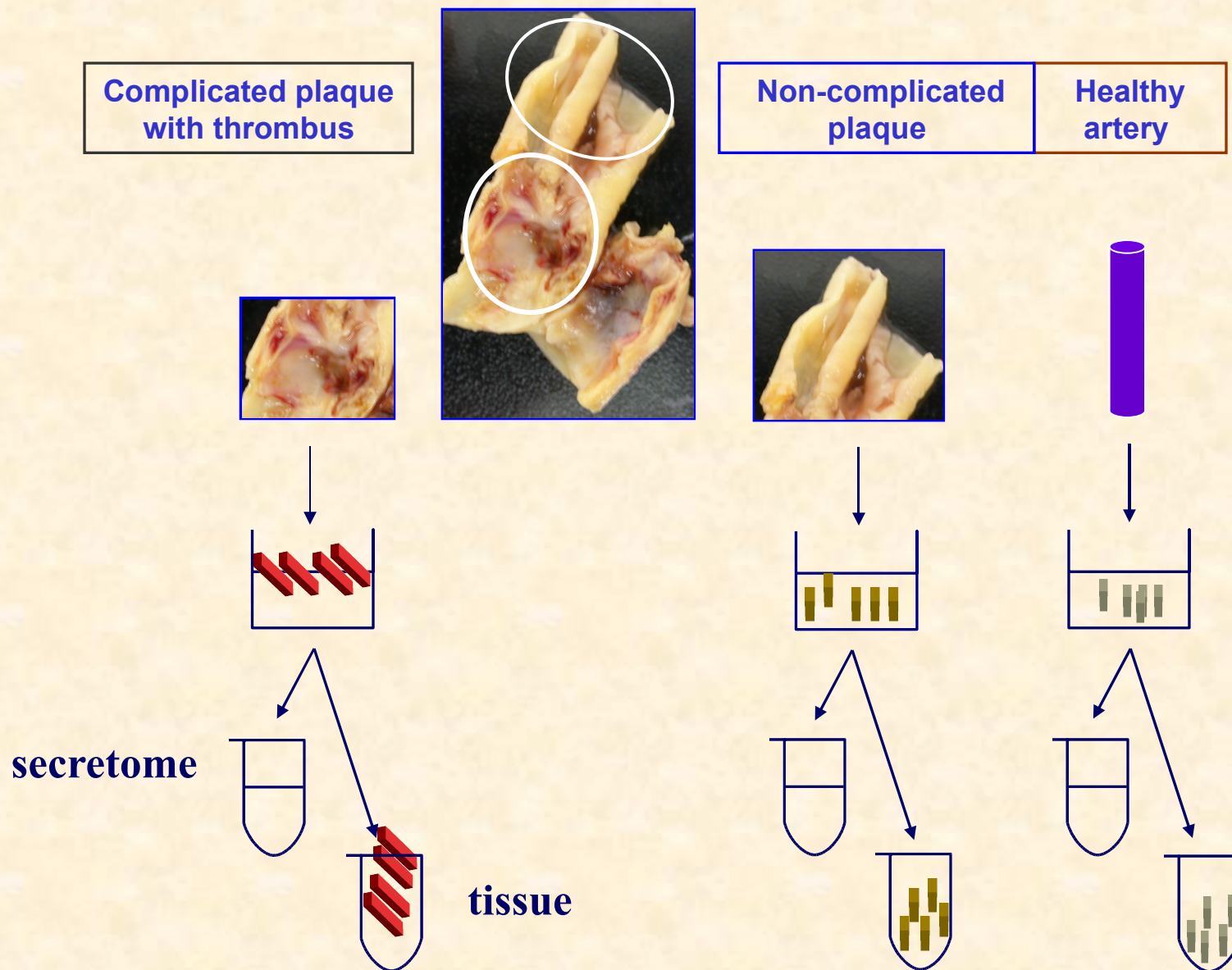


No. of Events	73,108	34,690	18,580	8,809	3,824
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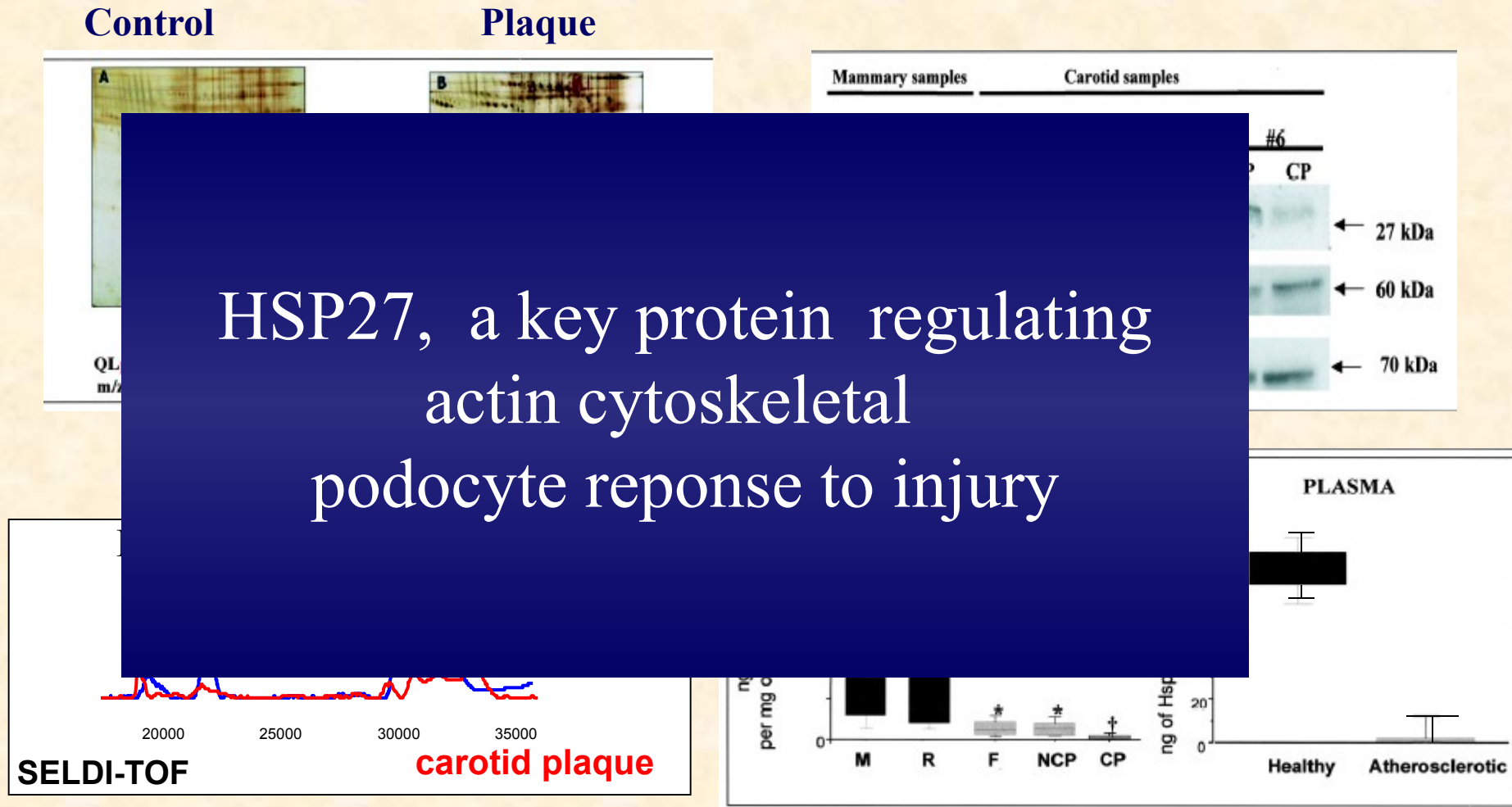
Proteomic approaches to the cardiovascular disease



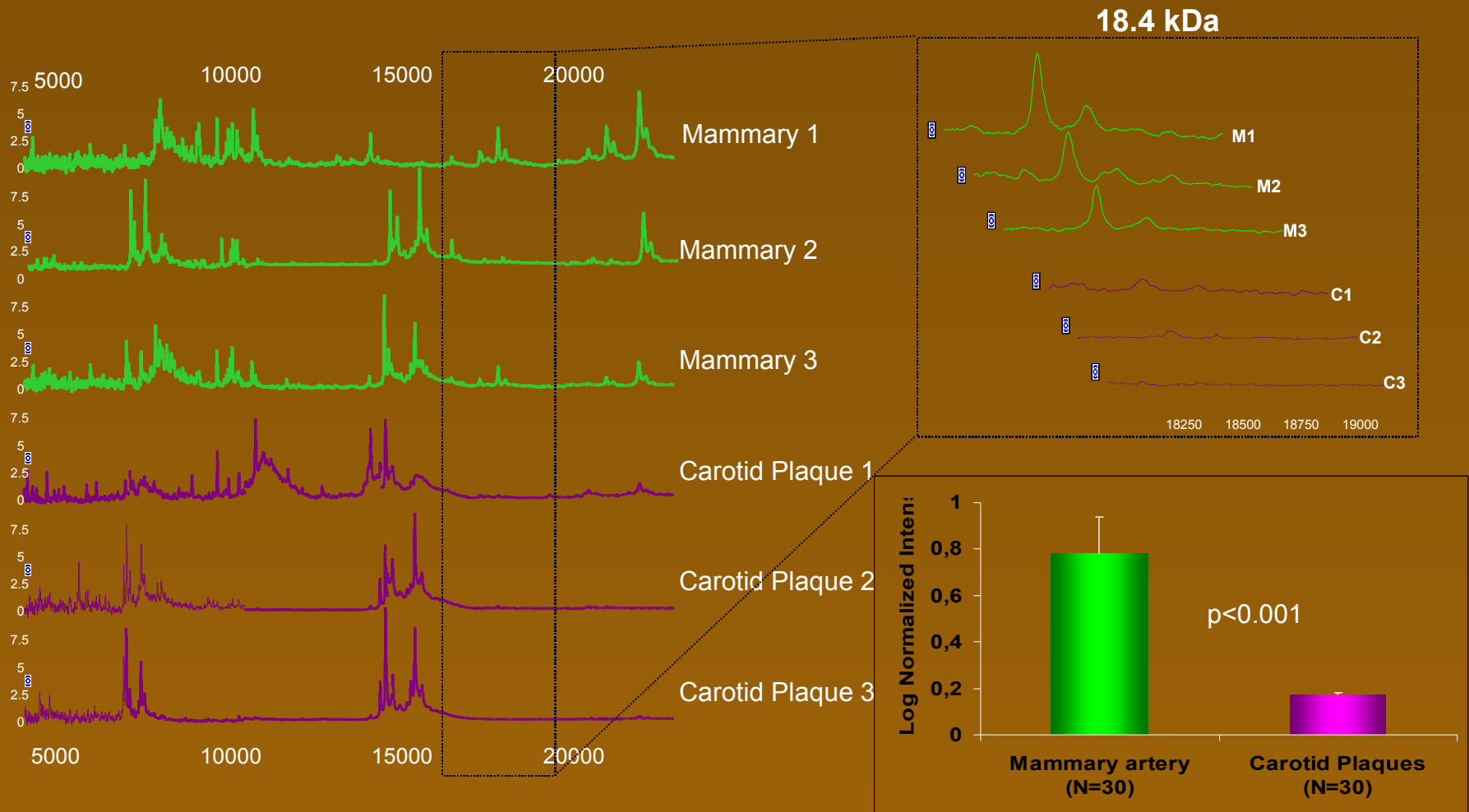
Proteomic analysis of human vessels in culture



Identification by a Differential Proteomic Approach of Heat Shock Protein 27 as a Potential Marker of Atherosclerosis



SELDI protein profiles in the supernatans of cultured human atherosclerotic plaques

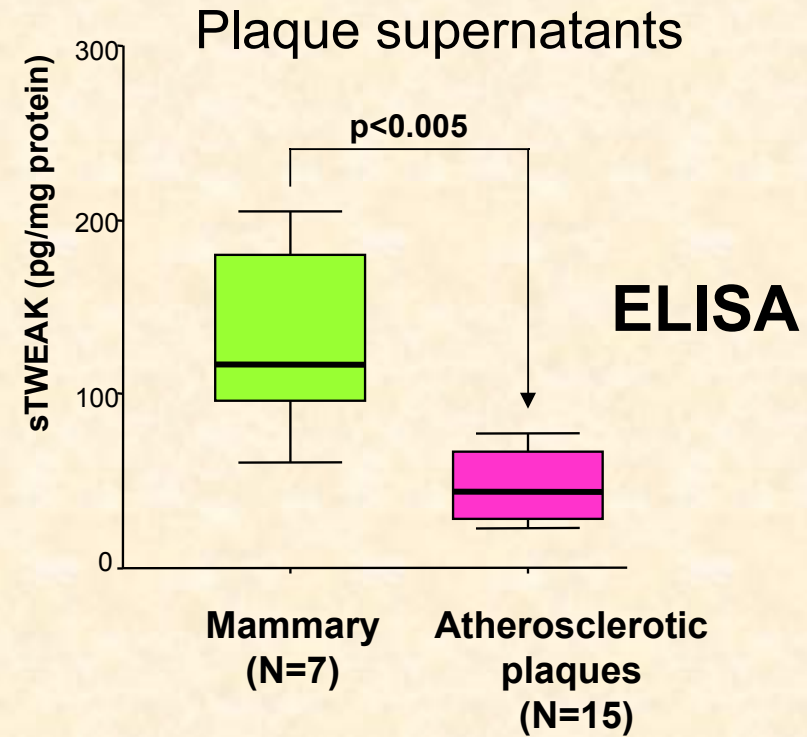
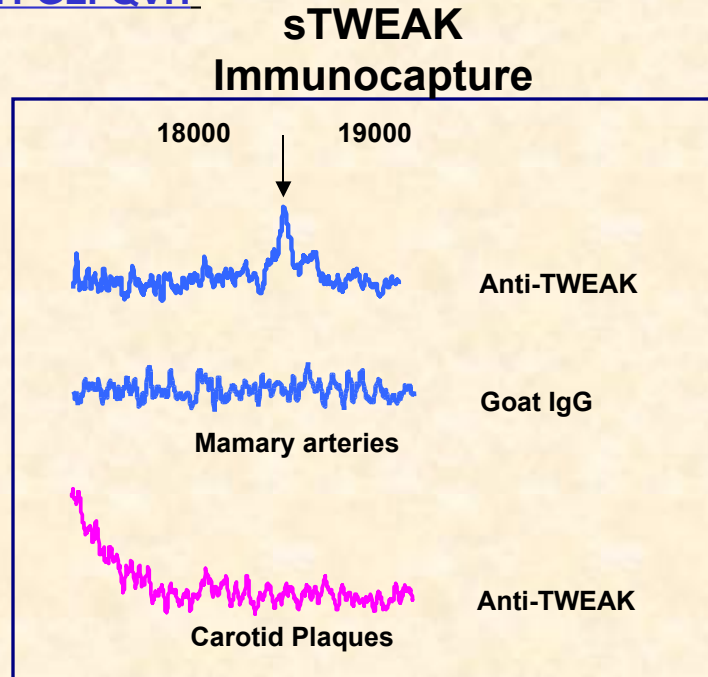


Identification by SELDI TOF-MS protein chip® of a 18.4 kda peak as soluble TWEAK (TNF-like weak inducer of apoptosis)

TNF superfamily, TWEAK. Secreted form 94-249 aa.

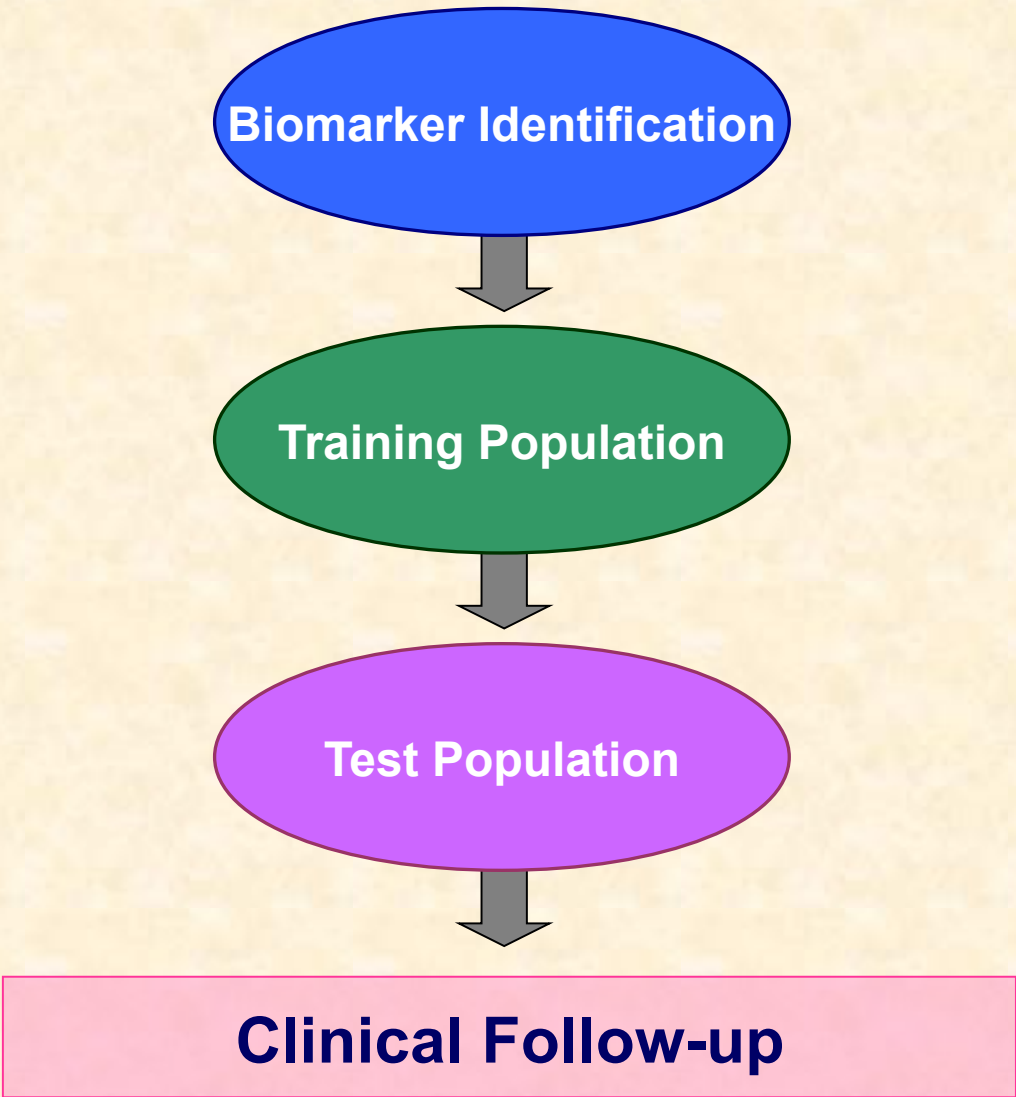
Score 76; p=0.001; Sequence Coverage: 56%

94 SAPKGRK TRARRIAAH YEVHPRPGQD GAQAGVDGTV SGWEARINS
141 SSPLRYNRQI GEFIVTRAGL YYLYCQVHFD EGKAVYLKLD LLVDGVLALR
191 CLEEFSAATAA SSLGPQLRLC QVSGLLALRP GSSLRIRTLP WAHLKAAPFL
241 TYFGLFQVH



Biomarker validation

Biomarker Identification



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graph TD; A([Biomarker Identification]) --> B([Training Population]); B --> C([Test Population]); C --> D[Clinical Follow-up];
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The diagram illustrates a four-step process for biomarker validation. It begins with 'Biomarker Identification' in a blue oval, followed by 'Training Population' in a green oval, and 'Test Population' in a purple oval. Each step is connected to the next by a downward-pointing grey arrow. The final step, 'Clinical Follow-up', is shown in a pink rectangular box at the bottom of the flow.



Training Population



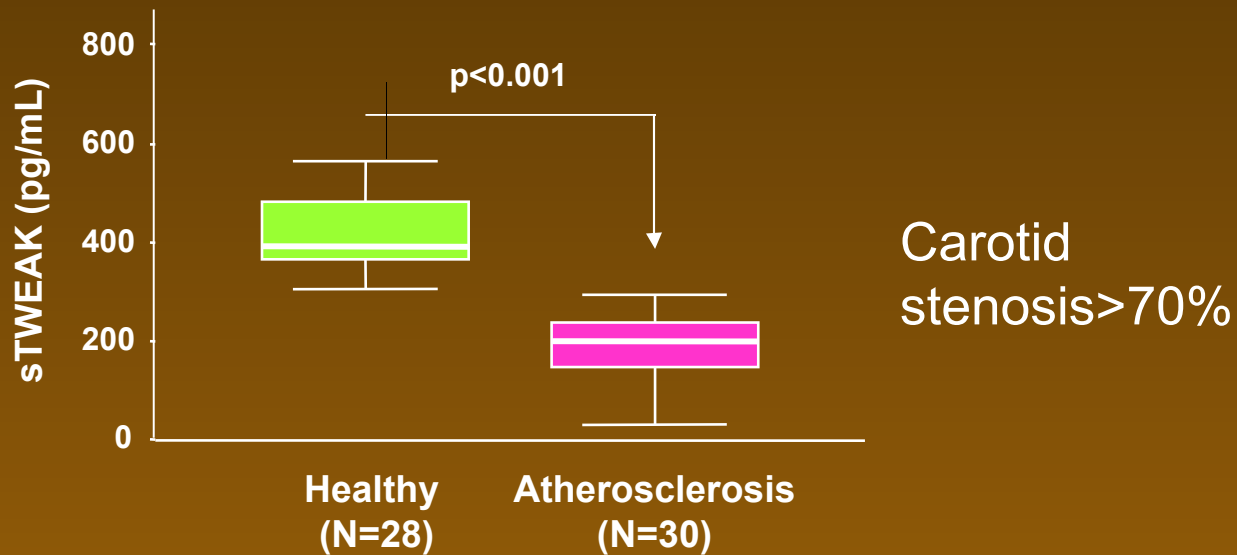
Test Population



Clinical Follow-up

Soluble TWEAK **plasma** levels are decreased in patients with atherosclerotic plaques

TRAINING POPULATION



sTWEAK Plasma levels negatively correlates with IMT in apparently healthy subjects

IMT=intima media thickness

Asymptomatic patients (N=106)

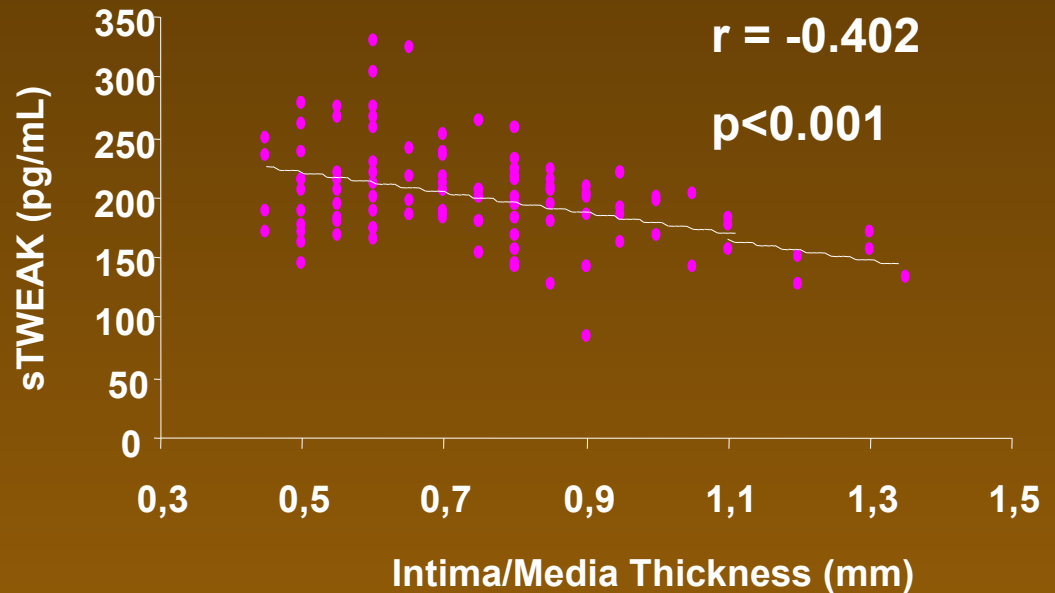
CRP $r=0.16$; $p=0.09$

Fibrinogen $r=0.29$; $p=0.01$

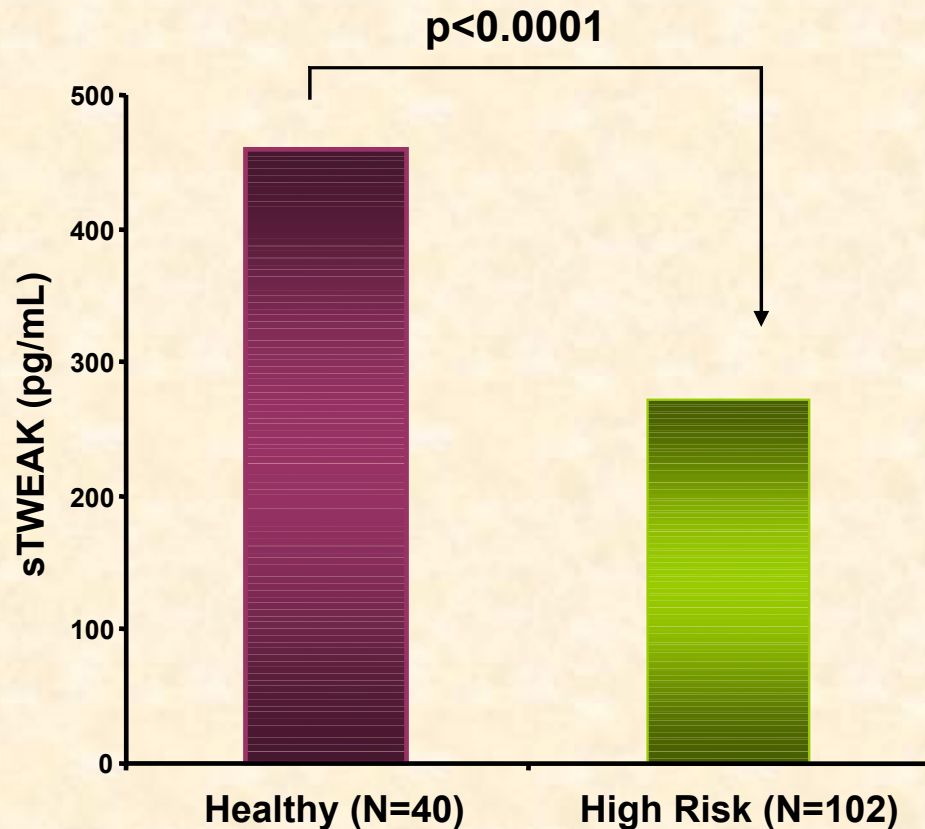
vWF $r=0.21$; $p=0.03$

The association between sTWEAK and carotid IMT remained significant after adjusting for traditional risk factors and inflammatory markers.

TEST POPULATION



TWEAK plasma levels are decreased in patients with high cardiovascular risk and metabolic syndrome

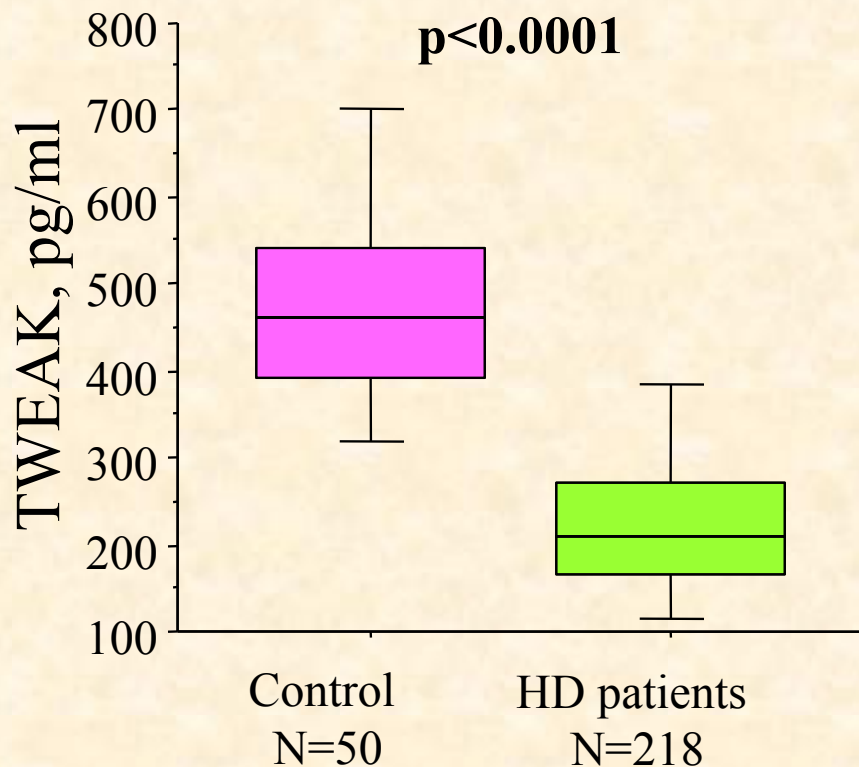


TWEAK, a new player
in the development
of **insulin resistance**

Feng F et al Endocrinology
149:1505-1513, 2008

Additive effects of soluble TWEAK and inflammation on mortality in hemodialysis patients

218 patients undergoing hemodialysis followed for 36 months (81 died)



- TWEAK plasma levels were a predictor of cardiovascular and all-cause mortality

- The association of TWEAK with

CRP ($\rho = -0.16$, $P = 0.01$)

IL-6 ($\rho = -0.17$, $P = 0.009$)

fibrinogen ($\rho = -0.20$, $P = 0.001$)

PROTEOMICS



Mas S, et al Proteomic Clin ,2007 ;1:1102-1122.

Conclusions

- The study of atherosclerotic plaques has allowed the identification of a number of candidate proteins, such as **HSP27** and **TWEAK**, of potential interest to kidney diseases.
- Vascular proteomics** should be included in the **EuroKUP** network as a fruitful field for searching novel renal biomarkers

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