

The background of the slide is a close-up, artistic rendering of several red blood cells. The cells are shown in various orientations, some in sharp focus and others blurred, creating a sense of depth. The color is a deep, vibrant red.

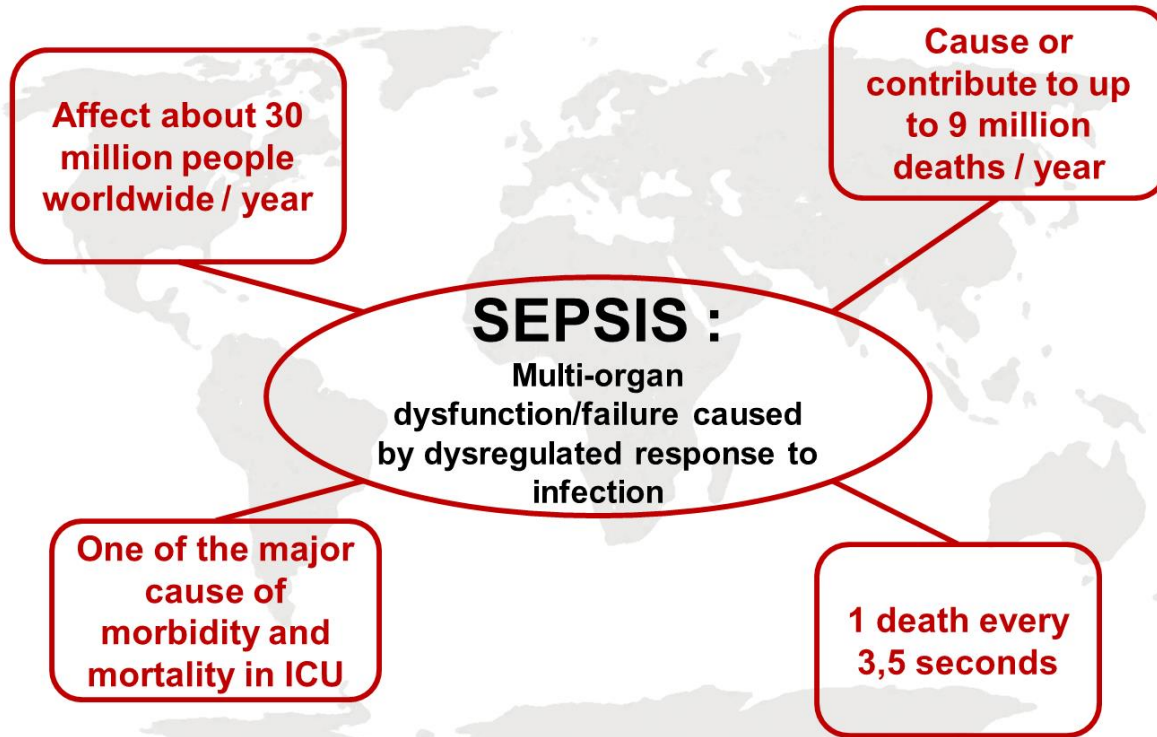
SEPTIMET

*Metrology to enable rapid and accurate
clinical measurements in acute management of
sepsis*

**SEPTIMET: metrology developments to
improve identification and treatment of
sepsis – Focus on Procalcitonin activities**

Dr Amandine Boeuf, LNE

SEPSIS



<https://www.worldsepsisday.org/>

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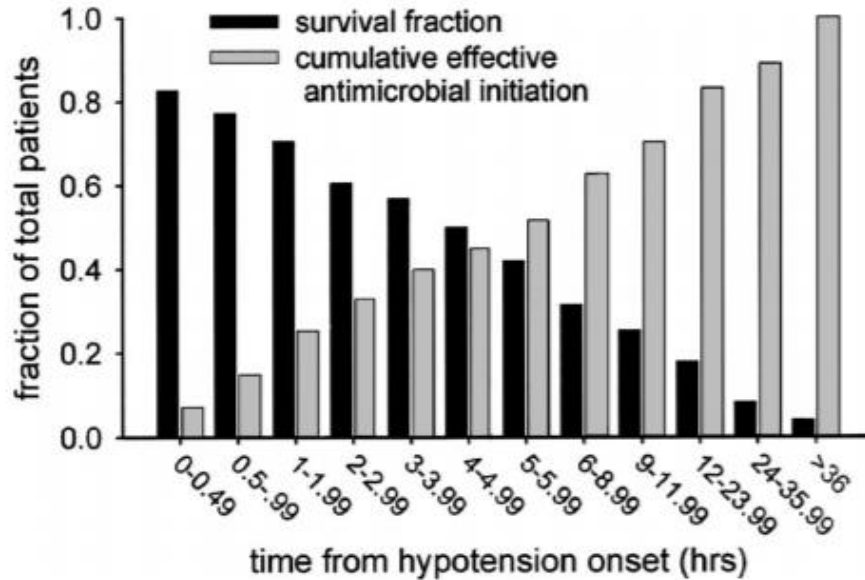
In 2017, **WHA** and **WHO**
made sepsis a global health
priority

→ resolution to improve the
**prevention, diagnosis and
management** of sepsis

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Patient outcomes and therapy : **the sooner the better!**



From Kumar et al. Crit Care Med 2006; 34: 1589-96

Diagnostic

≡

critical factor in
managing sepsis,

but **still a challenge** for
clinicians in ICU and
emergency departments

Metrology to enable rapid and accurate clinical measurements in acute management of sepsis

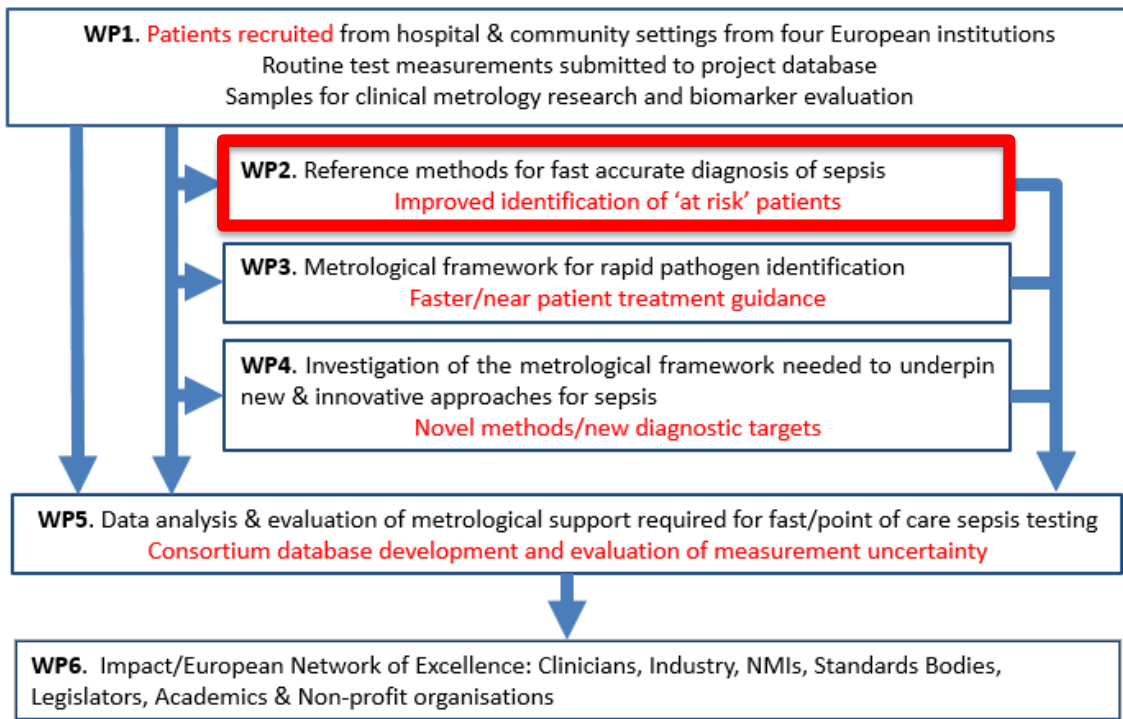
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Coordinator : Jim Huggett (LGC)

Start: September 2019

Objective:

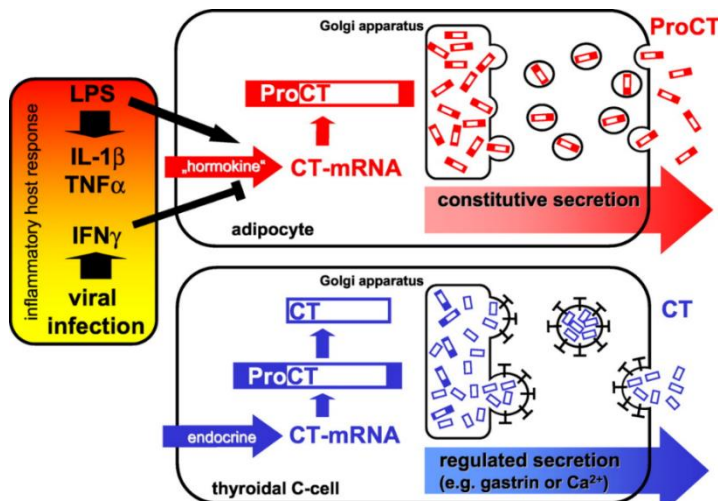
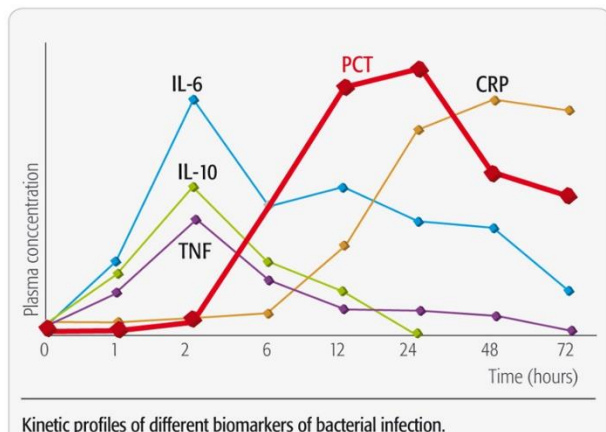
Improve the speed, accuracy and reproducibility of diagnostic tests for the identification and treatment of sepsis



Procalcitonin (PCT)

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- 116 amino acid polypeptide
- Precursor of calcitonin
- ↗ when bacterial inflammation
- Peak level achieved rapidly
- ↘ rapidly after end of injury



→ PCT concentration may rise to 100 ng/mL

→ Low PCT concentration (0.05 ng/mL)

From Lindscheid et al, Endocrinology, 2003;144(12):5578-5584

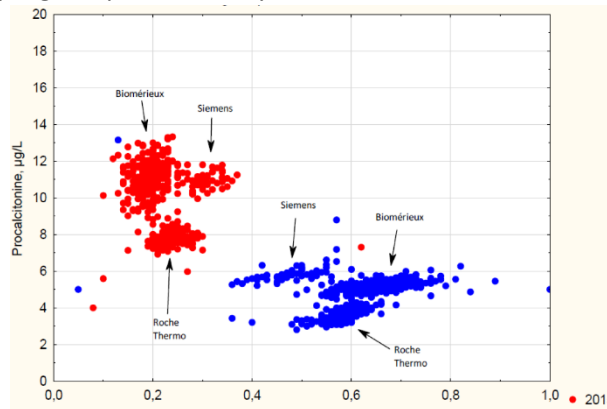
Specific biomarker for bacterial infection

Procalcitonin assays

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- Routine assays → Immunoassays
- No higher order reference measurement procedures
- No Certified Reference Materials

EQA program performed by ANSM in France in 2014 and 2015

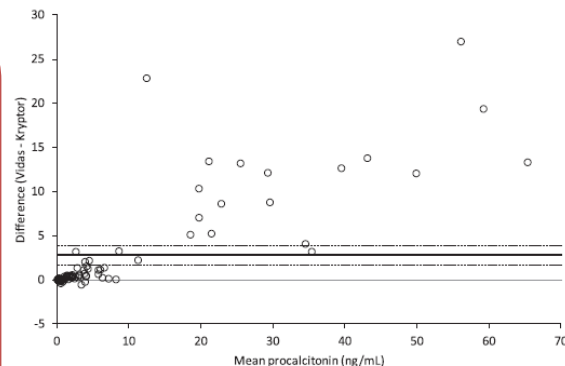


→ 17-20% between-methods RSD observed

**Need of
standardisation ?**

**→ Evaluate the
needs and
feasibility**

M. Dipalo et al. / Practical Laboratory Medicine 2 (2015) 22–28



→ Good correlation at low PCT level
(clinically relevant level)

IFCC working group on PCT standardisation

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Membership

Name	Position	
V. Delatour	Chair	FR
A. Boeuf	Member	FR
H. Briand	Member	FR
N. Corocher	Member	IT
A.M. Dupuy	Member	FR
P. Hausfater	Member	FR
P. Kaiser	Member	DE
Q. Liu	Member	SG
B. Machetanz	Member	DE
L. Pallavicini	Member	IT
S. Pastori	Member	IT
J. Pfannkuche	Member	DE
K. Schneider	Member	DE
P. Schütz	Member	CH
C. Tsatsanis	Member	GR
C. Yuan	Member	US
P. Bryan	Member/OCD	US
M. Grimmeler	Member/Diasys	DE
T. Masetto	Member/Diasys	DE
J. Odarjuk	Member/Thermo Fisher	DE
N. Parker	Member/Siemens	US
M. Patru	Member/OCD	US
K. Paulsen	Member/Beckman Coulter	DE
M. Rottmann	Member/Roche	DE
S. Ruetten	Member/Abbott	US
A. Rybin	Member/Siemens	US
L. Seaver	Member/Abbott	US
M. Solari	Member/Beckman Coulter	US
B. Thomas	Member/Thermo Fisher	DE

1/ Develop and validate a reference measurement procedure for PCT absolute quantification by IDMS to establish metrological traceability of results to the SI Units

2/ Document and understand the variability of results provided by the different commercially available PCT assays

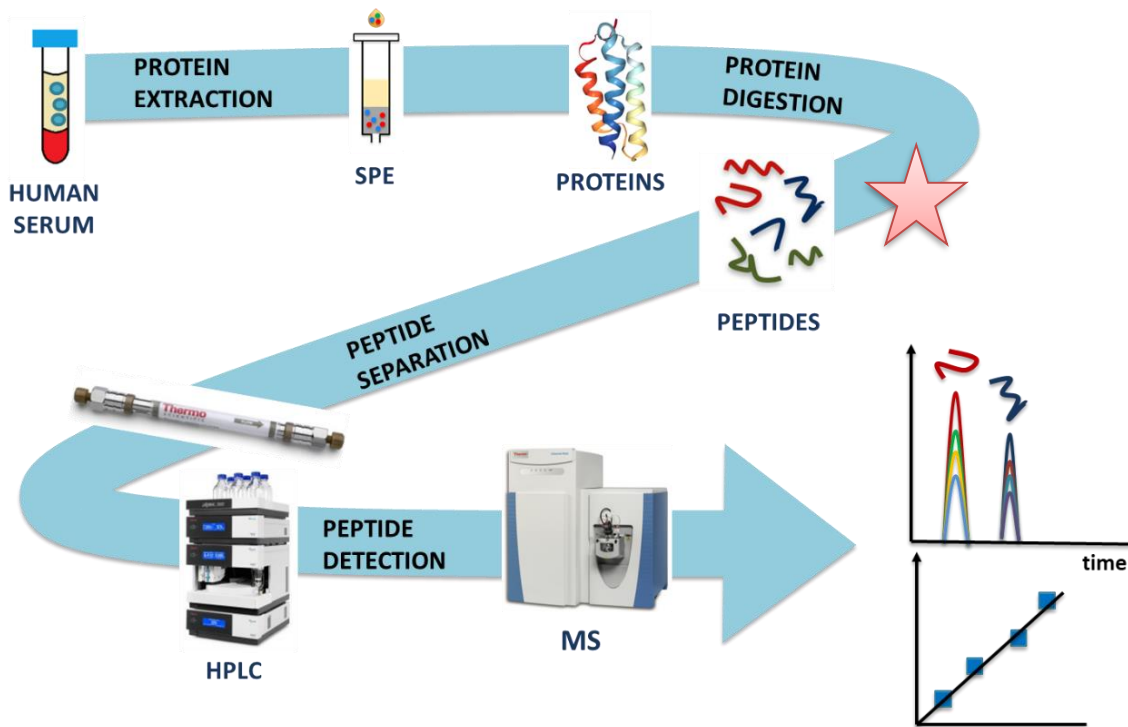
3/ Evaluate the feasibility for standardisation of PCT assays through common calibration with commutable calibrators

4/ If standardisation of PCT assays appears desirable and feasible:

- Produce commutable calibrators value assigned with the IDMS reference method
- Effectively recalibrate PCT assays
- Assess accuracy and comparability of PCT assays
- Evaluate the impact of assays recalibration

Procalcitonin

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Calibrators: **Synthetic peptides**

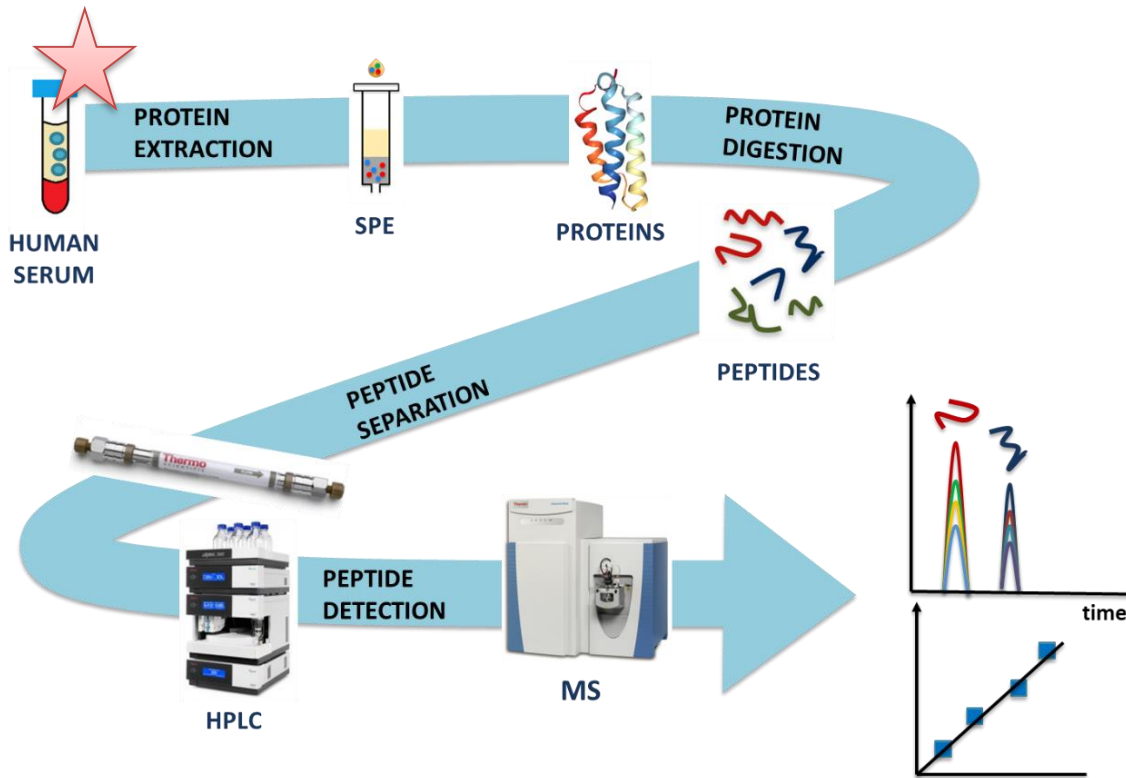
POSTER P-12: *Candidate reference method to establish traceable PCT measurement results*

Huu Hien Huynh *et al.*



Procalcitonin

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Calibrators: **recombinant protein**, supplied in 180 aliquots of 50 μ L

Characterisation of primary calibrator :

- Quantification by Amino Acid Analysis
- Impurity identification and quantification
- Correction of Amino Acid Analysis results

Amino Acid Analysis

first results

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ET D'ESSAIS



(secondment of H.H. Huynh in July 2019)

	Test 1 (from one aliquot)	Test 2 (from two aliquots)	Test 3 (from two aliquots)
Concentration ($\mu\text{g/mL}$)	865.3	721.4	789.9
Mean concentration ($\mu\text{g/mL}$)	792.2		
CV%	9.1		

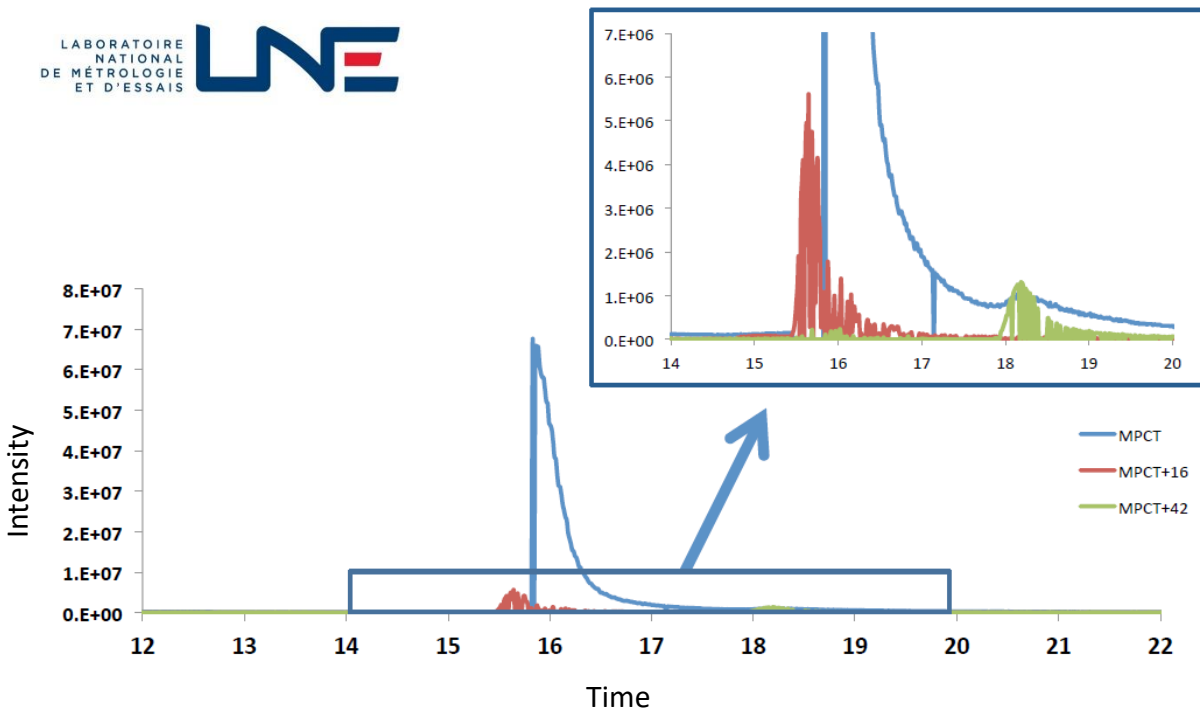
→ Homogeneity study on-going

Purity analysis (LC-MS)

first results

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U3000 / Q Exactive Focus (Thermo scientific)
Pepmap100 C18 column, 3 μ m, 1 x 100 mm
Mobile phase A: H₂O, 0.1% Formic Acid
Mobile phase B: ACN, 0.1% Formic Acid
T column: 25°C

Purity analysis (LC-MS)

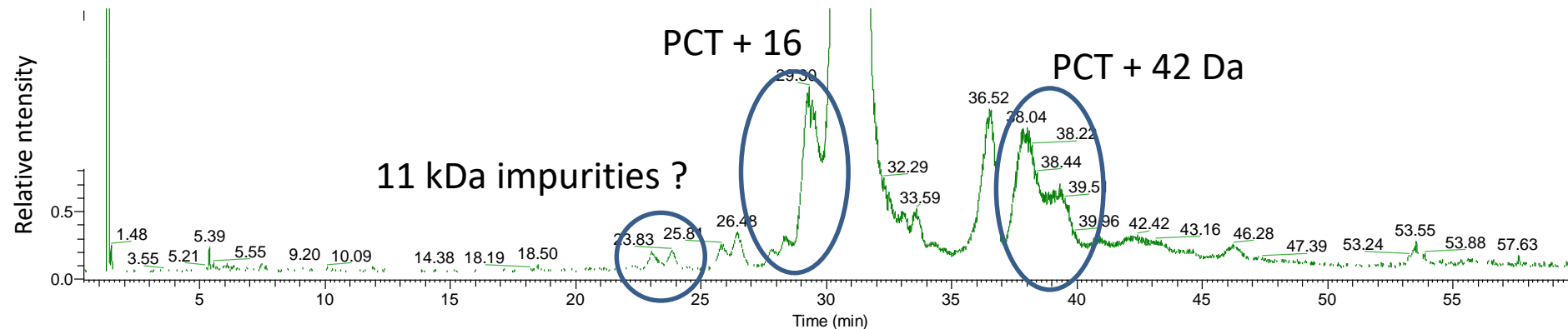
first results

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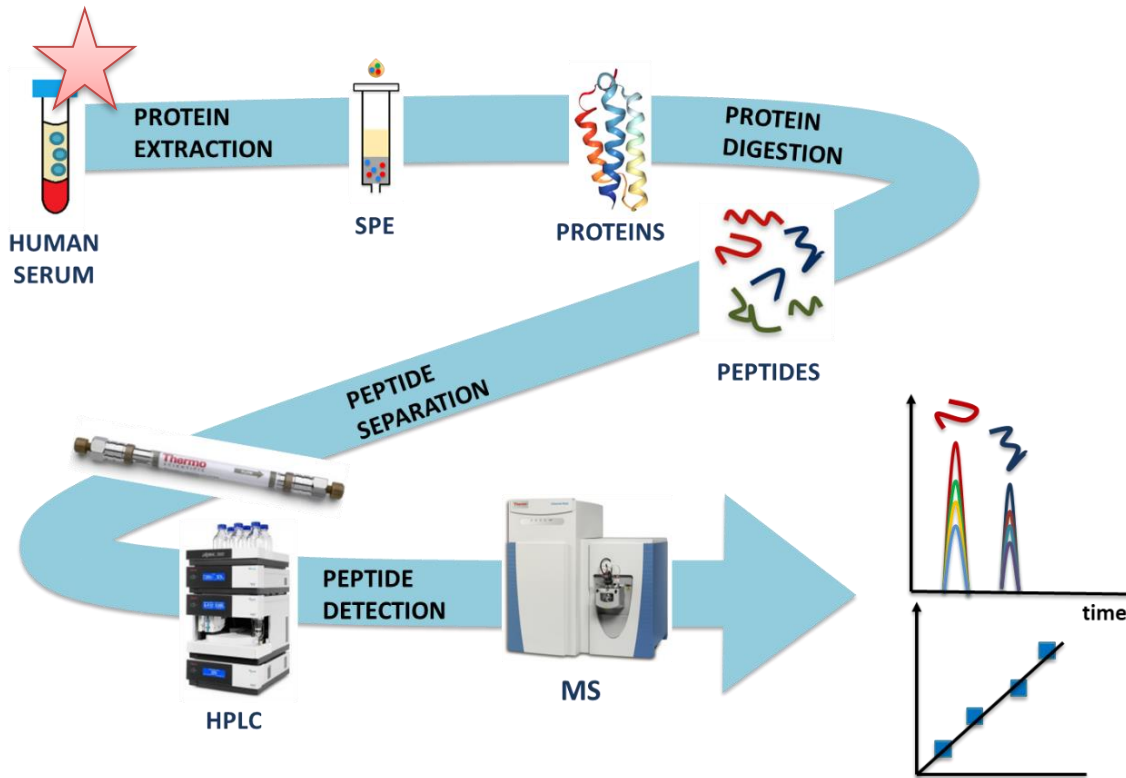
(secondment of A. Boeuf in Sept 2019)

Vanquish / Q Exactive Plus (Thermo scientific)
ACE 3 C4-300, 2.1 x 100 mm
Mobile phase A: H₂O, 0.1% Formic Acid
Mobile phase B: ACN, 0.1% Formic Acid
T column: 25°C



Procalcitonin

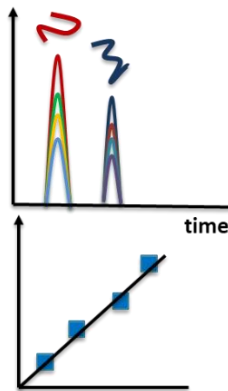
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Calibrators: **recombinant protein**, supplied in 180 aliquots of 50 μ L

Characterisation of primary calibrator :

- Quantification by Amino Acid Analysis
- Impurity identification and quantification
- Correction of Amino Acid Analysis results



Acknowledgments

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EMPIR



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Chiara Giangrande,
Béatrice Lalere,
Sophie Vaslin-Reimann

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