Development of reference materials to standardize microvesicle detection

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on behalf of Rienk Nieuwland[1]

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Disclosures for Edwin van der Pol

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Research Support/P.I.	**No relevant conflicts of interest to declare**
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Consultant	**No relevant conflicts of interest to declare**
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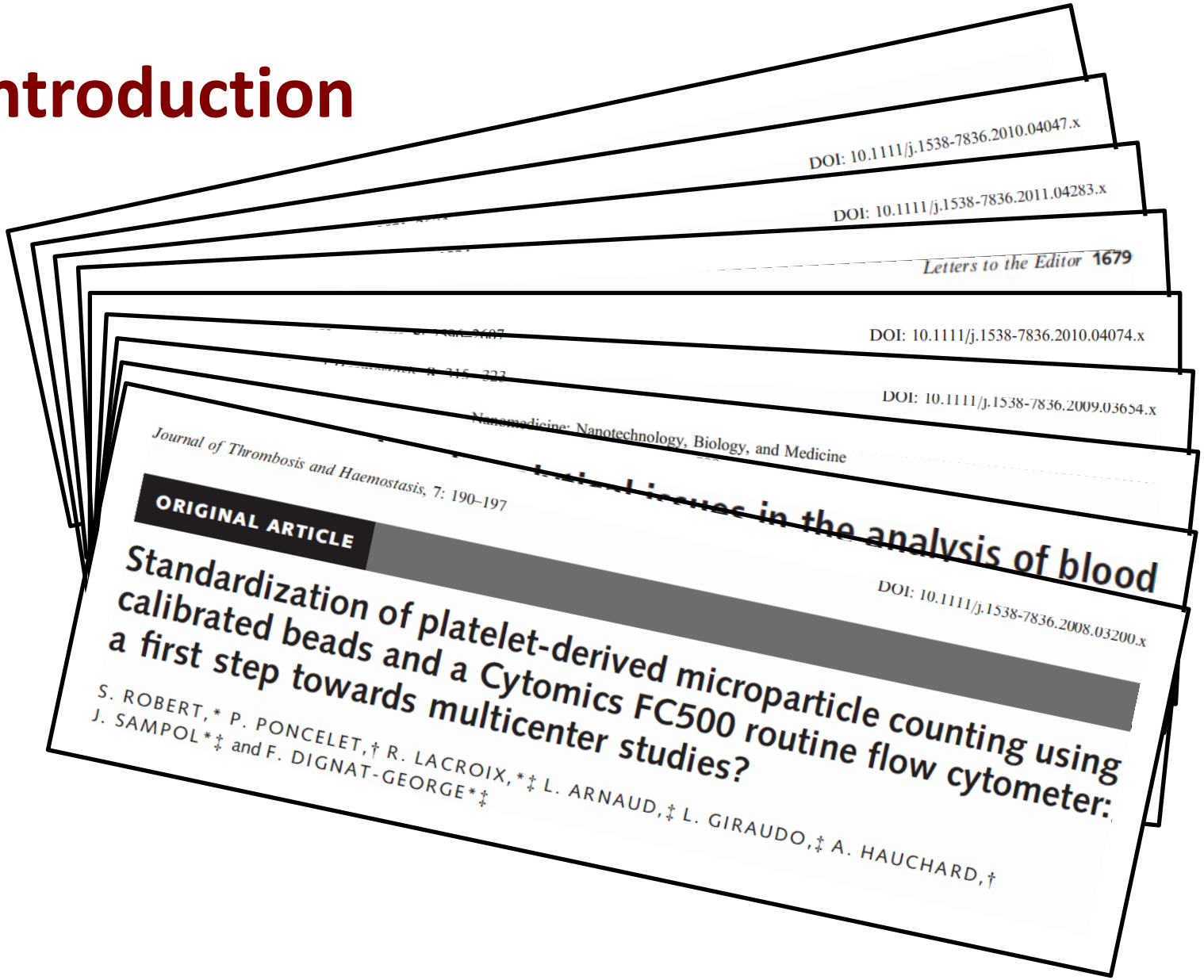
Scientific Advisory Board	**No relevant conflicts of interest to declare**

Presentation includes discussion of the following off-label use of a drug or medical device:
<N/A>

Introduction



Metrology for health call 2011

- support reliable and efficient exploitation of diagnostic and therapeutic techniques and development of new technologies to improve healthcare
- metrology is the science of measurement

VSL
Dutch Metrology Institute

Service
Metrologie
Metrologische
Dienst

PTB

Metrological characterization of microvesicles from body fluids as non-invasive diagnostic biomarkers

METAS
Federal Office of Metrology

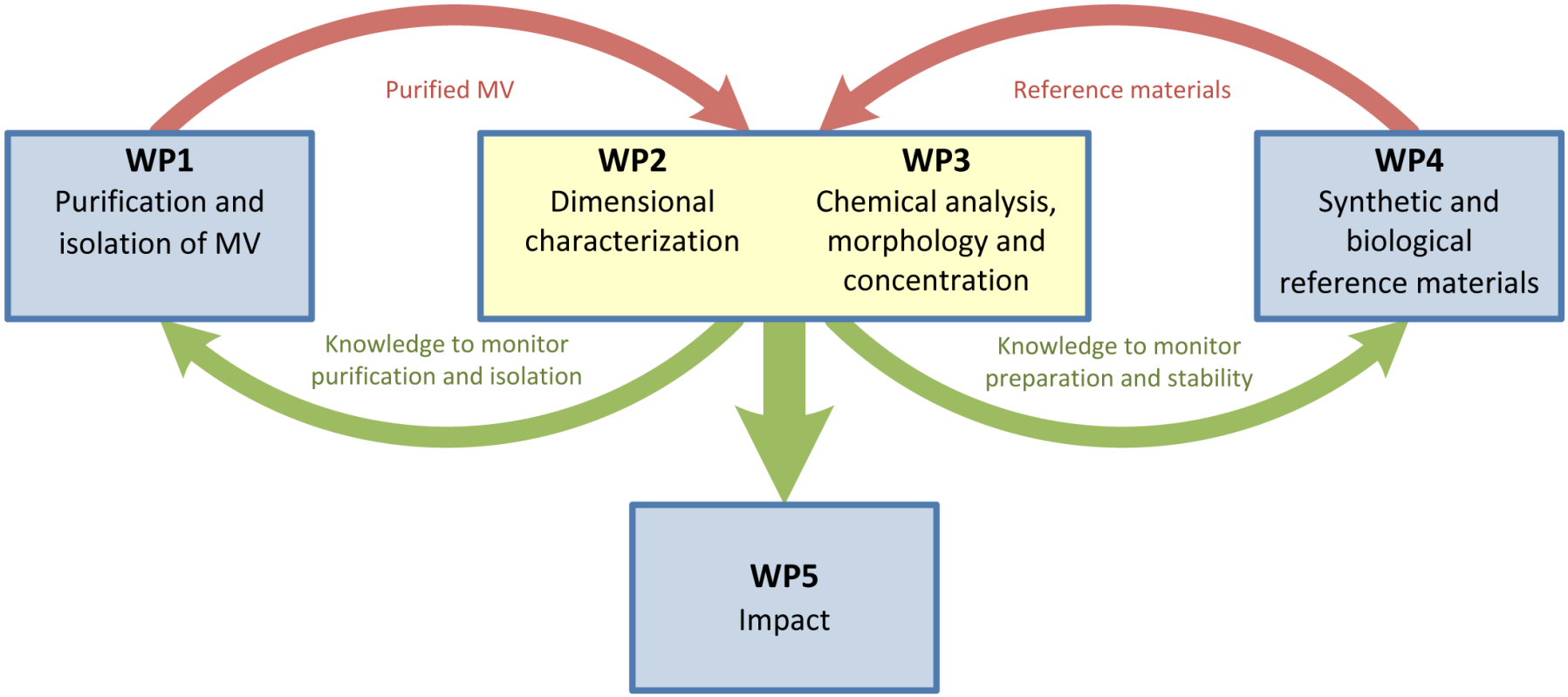
amc

Letters of Support

Aim

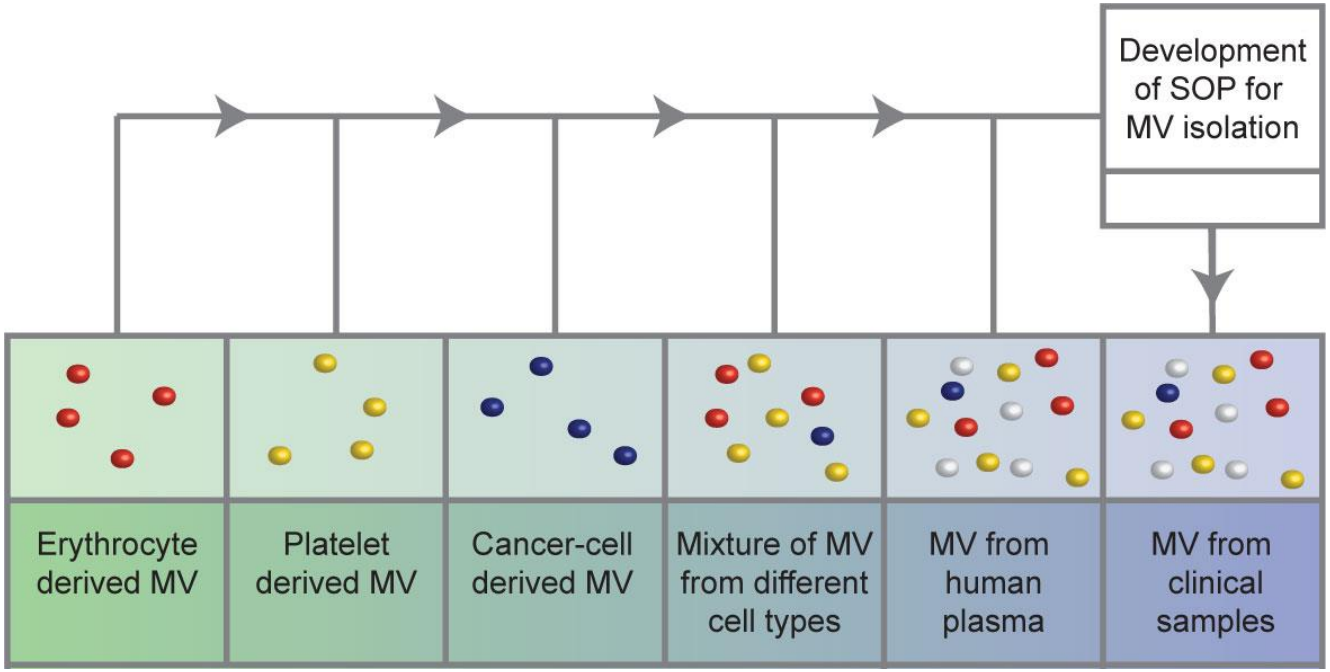
- develop reliable, comparable and quantitative analysis of microvesicles in biological fluids
  - development of isolation procedures
  - dimensional characterization
  - characterization of the chemical composition, morphology and concentration
  - selection, characterization and distribution of reference materials

Work packages



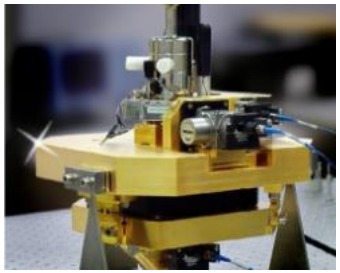
Work package 1

- development and application of procedures for microvesicle isolation



Work package 2

- dimensional characterization of microvesicles and reference materials
  - free in suspension (nanoparticle tracking analysis, resistive pulse sensing, small angle X-ray scattering)
  - adhered to a surface
    - dried conditions (atomic force microscopy, (transmission) scanning electron microscopy)
    - wet conditions (atomic force microscopy)



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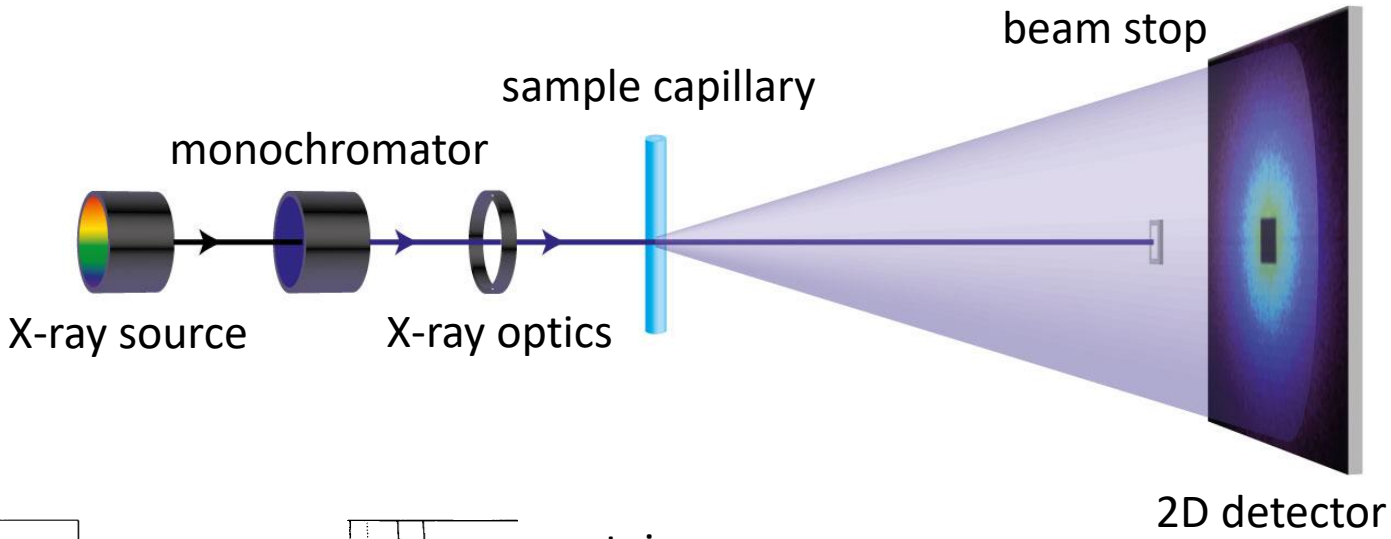
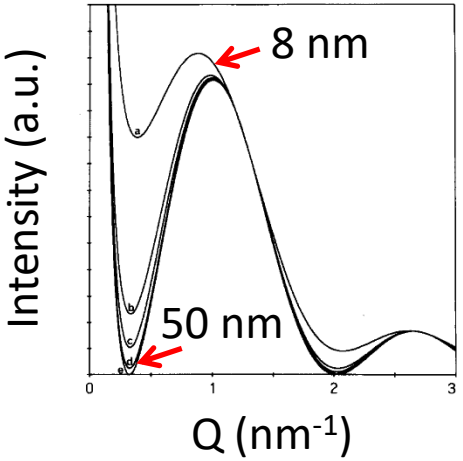
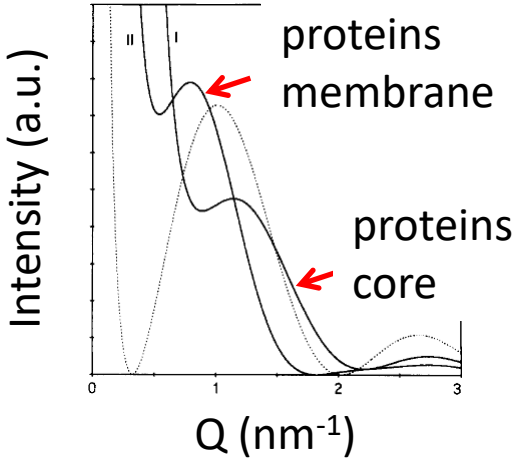
Small angle X-ray scattering







Calculations: Bouwstra et al. *Chem. Phys. Lip.* 1993

Work package 3

- chemical analysis, morphology, and concentration of microvesicles
  - chemical analysis (anomalous small angle x-ray scattering, X-ray fluorescence)
  - cellular origin and type (atomic force microscopy with functionalized tips)
  - morphology
    - dried conditions (atomic force microscopy, transmission electron microscopy)
    - wet conditions (atomic force microscopy)
  - concentration (nanoparticle tracking analysis, resistive pulse sensing)

Work package 4

- development and distribution of traceable reference materials

Reference material	Size (nm)	Concentration (ml^{-1})	Density (g/cm^3)	Refractive index @530 nm
Synthetic particles				
• polystyrene beads	30 – 1,000	$1x10^{10}$ – $1x10^{14}$	1.05	1.599
• silica beads	30 – 1,000	$1x10^{10}$ – $1x10^{14}$	2.00	1.461
biological particles				
• Intralipid	25 – 700	~$1x10^{14}$	0.93	1.465
• purified vesicles	30 – 1,000	variable	1.13-1.19	not known

- inter metrological laboratory comparison
- inter clinical laboratory comparison

Inter clinical laboratory comparison

- goal
  - validate developed protocols and detection methods in clinical laboratories using traceable reference materials
- distribution
  - September and December 2014
- data
  - collection and analysis in January and February 2015
- results
  - report and peer-reviewed article

Participation

To participate in this SSC survey, please send an e-mail to

r.nieuwland@amc.uva.nl

before October 1st 2012. Please include your

- name and affiliations
- available detection method(s)