

MeCAT – a new innovative technology for analysis and absolute quantification of proteins and peptides by mass spectrometry



Absolute quantification of proteins

Proteins are more and more important in development of modern diagnostics and drugs. Since a few years new protein analysis technologies allow a better identification and relative quantification of proteins, but there is still a lack in high sensitive absolute protein quantification. MeCAT is a new patented technology of Proteome Factory which allows absolute quantification of proteins and biomolecules using ICP-MS (Inductively Coupled Plasma Mass Spectrometry) first time. The biomolecules are labelled by MeCAT reagents which contain metals (lanthanides).

Example 1:

A protein drug x is present at a low concentration in a medicinal drug. Other proteins like human albumin are also present in much higher concentration to stabilize etc. protein drug x. There is a problem to determine the exact amount of drug x by classical protein concentration determination methods in a single dose of the drug. HPLC, total amino acid hydrolysate determination or protein quantification by Bradford or other assays can only detect the total protein concentration or are not sensitive enough, respectively. First time MeCAT allows the absolute quantification of protein drugs of very low amount even if other proteins are present in much higher amount due to absolute quantification of MeCAT-metal tagged proteins by LC-ICP-MS. ICP-MS is a very sensitive quantification technology for metals (e.g. commonly used in environmental analysis) with a extraordinary dynamic range of at least 10^9 . By combination of MeCAT tagging with LC separation and ICP-MS it is possible to detect and absolute quantify proteins in the attomol range which is at least some orders of magnitude more sensitive than LC-UV detection. Standard metal solutions are used for calibration.

MeCAT for absolute quantification of proteins
(e.g. protein containing drugs/ ratio drug : albumin $\rightarrow$ 1 : 10000)

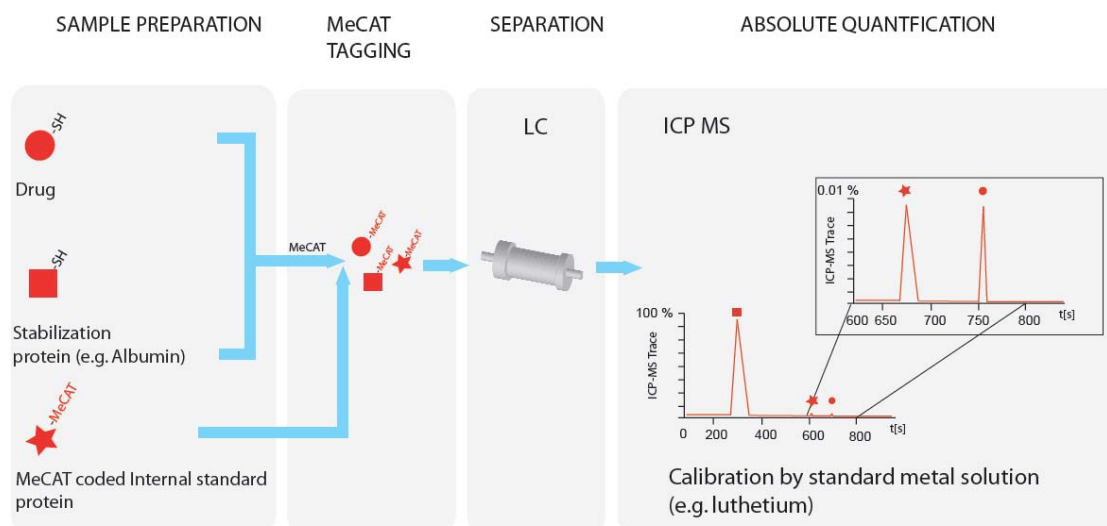


Figure 1: MeCAT-Technology for absolute Protein Quantification

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Example 2: Biomarker- and Target-Finding

MeCAT technology is compatible to common protein and peptide separation techniques (e.g. electrophoresis, LC) as well as to mass spectrometry for biomolecules (MALDI-MS, ESI-MS). By using different metals bound to MeCAT for labelling of several protein containing samples quantitative multiplex analysis of these samples is possible comparable to stable isotopic labelling techniques. **But MeCAT is much more powerful.** It is the next generation of protein tagging technology for quantitative proteome and protein analysis because the MeCAT metals can be quantified in an absolute way by using ICP-MS and external metal standard solutions. MeCAT allows the absolute quantification of proteins as well as peptides in multiplex analysis. Furthermore analysis to analysis variation can be minimized by introduction of complex internal protein or peptide standards which are labelled with an additional metal.

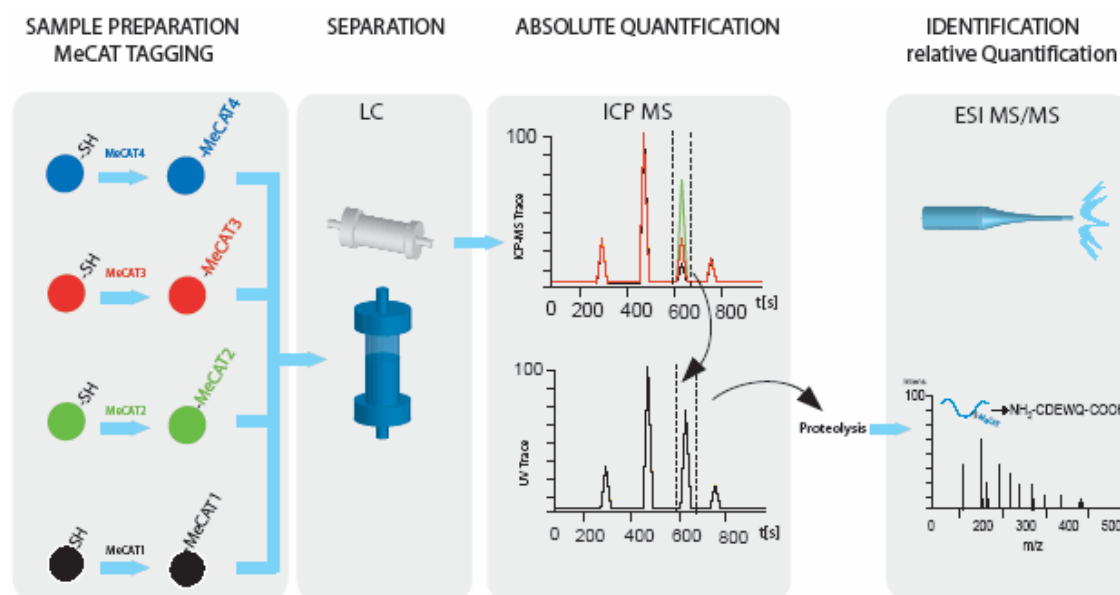


Figure 2: MeCAT-Technology for Multiplexing Proteome Analysis

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MeCAT overview

- Absolute quantification of proteins and peptides in
 - o drug
 - o diagnostics
 - o other protein containing products
- Absolute Quantification of other biomolecules (DNA, RNA, carbohydrates, lipides etc.) in drugs, diagnostics or other protein containing products
- Biomarker- and Target-Screening

Advantages

- First time absolute quantification of biomolecules by using metals
- Extreme sensitive detection of metals
 - ⇒ introduction of ICP-MS for routine bioanalytics
 - ⇒ unrivalled linear dynamical detection range (up to 9 orders of magnitude)
 - ⇒ extreme sensitive quantification of biomolecules (attomol range)
- Multiplex analysis of several samples at the same time possible
 - ⇒ Reduction in costs and time
- Internal standards for quality assurance
- Compatible with common mass spectrometers for protein and peptide identification and relative quantification (MALDI-MS, ESI-MSMS)
- Compatible with common protein and peptide separation technologies (electrophoresis, LC etc.)

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