

## **GOOD NEWS FOR MALDI THE ADVENT OF SECOND GENERATION MATRICES**

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All MALDI matrices in use until now have been found empirically following some straightforward and simple selection criteria, despite strong efforts and some progress to elucidate the underlying physicochemical principles. In a new approach, we synthesized numerous derivatives of the most widely used  $\alpha$ -cyano-4-hydroxycinnamic acid. Based on MALDI experiments two main functions were found to specify a well-working matrix, 1<sup>st</sup> a carboxylic group (attributed to play a role in analyte incorporation) and 2<sup>nd</sup> a high yield of protonated matrix ions. The latter points to the decisive role of matrix ions as protonating agents in a chemical ionization process. Increasing the gas-phase acidity was thus the step to design a superior matrix – successfully achieved by introducing a chlorine residue at the 4-position. The new matrix is highly superior both in the absolute peptide signal intensities detected, but also shows substantially less discrimination for peptides of lower basicity – thus facilitating both higher detection sensitivity and improved sequence coverage in proteomics experiments.