

Identification of Insulin Like Growth Factor 1 (IGF1) Variants Using High-Resolution Accurate-Mass Mass Spectrometry (HRAM-MS)

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Insulin like growth factor 1 (IGF1) is the preferred biomarker for the diagnosis of growth hormone (GH) deficiency and for monitoring response to GH treatment. Normal or high IGF1 concentrations in patients with IGF1 variants (V-IGF1) measured by current immunoassays have been reported. We demonstrate how HRAM-MS identifies V-IGF1 which immunoassays identify as wild-type IGF1. In our validation studies for high-resolution accurate-mass mass spectrometry (HRAM-MS) assay for IGF1 we observed that in 10 out of 1720 patients half of IGF1-IA was V-IGF1 (**Figure 1**). The objective of the present study was to characterize the V-IGF1 using a second (clinical) cohort of samples.

In our clinical cohort of 760 patients, we have identified five patients with V-IGF1. The overall frequency of occurrence of the V-IGF1 in two cohorts was 0.60%. The m/z used to quantitate the wild-type IGF1 was 1093. The V-IGF1 was found to have a same retention time at the native IGF1 and m/z difference ($\Delta m/z$) of ~ 4.5 Da. The IGF1-MS and IGF1-IA concentrations and the mass spectrum of V-IGF1 have been shown in **Figure 1**. Identification of V-IGF1 may be of clinical value especially for patients exhibiting GH resistance or IGF1 mutations as the dose of rGH can be tailored based on true IGF1 concentration in these patients.

Further LC-MS/MS studies to quantitate and characterize the V-IGF1 are underway. This presentation will describe the identification, characterization of V-IGF1. MS/MS data on V-IGF1 will also be presented.

Figure 1: (a) Method comparison between IGF1-IA and IGF1-MS in samples without the IGF1 variant (V-IGF1) (●;N=2465) and with V-IGF1 (●;N=15); (b) Extracted ion chromatogram of a sample containing the V-IGF1.

