Identification of Circulating IGF-1 Polymorphisms by High Resolution LC-MS

Background
- Insulin-like growth factor-1 (IGF-1) is an anabolic hormone and a biomarker for certain growth disorders.¹
- A high resolution liquid chromatography-mass spectrometry (LC-MS) assay that is highly specific for IGF-1 was developed at Quest Diagnostics.¹
- Reports in the literature have indicated that similar assays are able to identify single-amino-acid changes in IGF-1.²
- **Objective:** The investigators examined whether the IGF-1 LC-MS assay developed at Quest is capable of detecting single-amino-acid changes in IGF-1 in clinical samples.

Methods
- A search of the dbSNP and 1000 Genomes databases was conducted to identify genetic changes (single-nucleotide polymorphisms [SNPs]) that could affect IGF-1 protein size.
- LC-MS spectra from patient samples were retrospectively analyzed for molecules with a single-amino-acid substitution in the IGF-1 protein.

Results
- The database search identified 5 IGF1 SNPs that result in an amino-acid change, with minor allele frequencies as follows:
  - A67T: 0.4% MAF
  - A70T: 0.04% MAF
  - V17M: 0.02% MAF
  - V44M and P66A: single reported incidences
- Analysis of existing LC-MS spectra indicated that multiple spectra were consistent with IGF-1 molecules containing single-amino-acid substitutions.

Conclusions
- The previously developed high-resolution LC-MS assay for IGF-1 is capable of identifying IGF-1 molecules with single-amino-acid substitutions.
- The identification of particular IGF-1 changes could affect the interpretation of test results for some patients.

References