ANALYSIS OF THE DIFFERENCES IN PROTEIN EXPRESSION ASSOCIATED WITH THYROID ORBITOPATHY USING THE PROTEOMIC APPROACH

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Purpose: Applying proteomics to understand the qualitative differences in protein expression of extraocular muscle tissues and orbital adipose tissues associated with thyroid orbitopathy (TO)

Material and method: For the study group, we obtained extraocular muscle tissues or orbital fat tissues from patients with thyroid orbitopathy during strabismus surgery or orbital decompression. For the control group, we also acquired extraocular muscle tissues from patients who had received strabismus surgery or took orbital fat tissues from patients who had accepted eyelid plasty. This study used two proteomic methods to comprehensively examine the extraocular muscle and orbital fat proteomes of TO patients and non-TO controls. These methods included two-dimensional gel electrophoresis (2-DE) combined with electrospray ionization – quadrupole – time-of-flight tandem mass spectrometry (ESI- QUAD-TOF MS/MS) and liquid chromatography tandem mass spectrometry (LC-MS/MS).

Result: Among all protein spots separated by 2DE, we found eight spots significantly differed between the study and control group. The eight spots were analyzed by ESI- QUAD-TOF MS/MS. Proteins from four of the eight spots were identified successfully, which had relatively higher concentrations in the study group. These were (1) chain A, human serum albumin in a complex with myristic acid and tri- iodobenzoic acid (2) chain B, structure of hemoglobin in the deoxy quaternary state with ligand bound at the alpha haems (3) beta globin chain variant and (4) chain A, structure of hemoglobin in the deoxy quaternary state with ligand bound at the alpha haems. To increase protein identification, we employed a complementary analytical platform, LC-MS/MS. Using this instrument, 7 proteins were identified only in the orbital fat tissues of the study group, including (1) chain A, human serum albumin in a complex with myristic acid and tri-iodobenzoic acid (2) chain B, human hemoglobin D Los Angeles: crystal structure (3) hemoglobin beta (4) chain B, structure of hemoglobin in the deoxy quaternary state with ligand bound at the alpha haems (5) beta globin chain variant (6) chain A, cyanomet Rhb1.1 (recombinant hemoglobin) and (7) an unnamed protein product. One protein—vimentin— was identified in the orbital fat samples of the non-TO controls, and this protein had significantly expressed in the control group. There were 10 proteins identified only in the extraocular muscle tissues of the study group, including (1) chain A, human serum albumin in a complex with myristic acid and tri-iodobenzoic acid (2) chain B, human hemoglobin D Los Angeles: crystal structure (3) beta-globin (4) hemoglobin beta (5) chain A, structure of hemoglobin in the deoxy quaternary state with ligand bound at the alpha haems (6) chain B, structure of hemoglobin in the deoxy quaternary state with ligand bound at the alpha haems (7) beta globin chain variant (8) chain B, crystal structure of human hemoglobin E at 1.73 A resolution (9) unnamed protein product (10) beta globin chain.

Conclusion: The results obtained with this proteomic analysis show which proteins are up-regulated or down-regulated in thyroid orbitopathy. This will be useful in understanding the pathophysiology of thyroid

orbitopathy as well as in finding candidates as new diagnostic biomarkers of thyroid orbitopathy.

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