Mitochondrial proteins as Parkinson’s Disease circulatory biomarkers – a translational study

Sandra I. Anjo1,2, Patrícia Valério dos Santos3, Maria Luiza Constante Rosado4,5, Graça Baltazar4, Mário Grãos1,6, Bruno Manadas1

1 Center for Neuroscience and Cell Biology, UC, Coimbra, Portugal; 2 Faculty of Medicine, UC, Coimbra, Portugal; 3 Centro Hospitalar de Setúbal, Setubal, Portugal; 4 Faculty of Health Sciences, UBI, Covilhã, Portugal; 5 Centro Hospitalar Cova da Beira, E.P.E., Covilhã, Portugal; 6 Biocant, Biotechnology Transfer Association, Cantanhede, Portugal

For more information please contact: sandra.isabel.anjo@gmail.com

1. Introduction:

The identification of circulating biomarkers that closely correlate with Parkinson’s Disease has failed several times in the past. Nevertheless, using a translational approach we could monitor two mitochondrial-related proteins in plasma samples, which in combination lead to a powerful model with potential diagnostic value to discriminate the PD patients from matched controls.

2. Strategy and Results:

This translational approach was initiated by the analysis of secretomes from cells cultured under control or oxidative stress conditions, from which several mitochondrial-related proteins were found to be released in higher amounts under oxidative stress. This screening, performed by SWATH-MS, was translated to the analysis of plasma samples from 28 control and 31 PD patients, and two of these proteins were found to be significantly changed in PD cohort.

3. Evaluation in plasma samples

2.3 Evaluation in plasma samples

A) Cohort characterization

<table>
<thead>
<tr>
<th>Gender</th>
<th>Patients group (n=31)</th>
<th>Control group (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>72.52 ± 6.71 (95.54%)</td>
<td>68.16 ± 10.09 (59.38%)</td>
</tr>
<tr>
<td>F</td>
<td>75.35 ± 7.25 (94.76%)</td>
<td>66.00 ± 9.85 (40.68%)</td>
</tr>
<tr>
<td>Total</td>
<td>73.79 ± 7.00 (97.28)</td>
<td>67.28 ± 9.78 (40.68)</td>
</tr>
</tbody>
</table>

B) biomarker discovery pipeline applied to plasma samples

5 µl of plasma

Protein Precipitation

Short GeLC-SWATH-MS analysis

B) Data analysis – Selection of Mitochondria-associated proteins

C) LDA analysis the mitochondrial-associated proteins

A linear discriminant analysis of the results obtained for these two proteins originates a model with potential diagnostic value to discriminate PD patients from matched controls. The model obtained has a specificity of 77.4%, a sensitivity of 78.6%; cross-validation of 76.3% and a ROC analysis with an area under the curve (AUC) of 0.872 (p<0.001).

4. Conclusions & Discussion:

Two mitochondrial proteins were associated with apoptotic mitochondrial changes, which may correspond to potential indicators of cell death and have never been reported as blood biomarkers for PD. In fact, to the best of our knowledge, one of these proteins was identified in plasma samples for the first time, and the other protein was already reported to be altered in as Alzheimer’s patients but not in PD patients. In this sense, we believe that the novelty and success of our results arise from the combination of: i) a translational research pipeline, where plasma samples were interrogated with previous knowledge from cell secretome under oxidative stress, and ii) the use of the quantification approach SWATH-MS associated with the use of a biofluid optimized normalization method.

5. References:


6. Acknowledgments:

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