Urinary neopterin as a potential biomarker for Motor Neuron Disease

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INTRODUCTION & AIMS

Objective markers of disease progression and prognosis are advantageous in assessing treatment effectiveness in clinical trials. Our laboratory discovered urinary p75<sup>ECDD</sup> as a biochemical marker that changes as disease progresses<sup>1</sup> and can be used to test treatment efficacy<sup>2</sup> in Motor Neuron Disease (MND). Using p75<sup>ECDD</sup> in a urinary biomarker panel with additional candidates will help to subgroup patients in trials, improve efficacy detection, and increase understanding of disease processes.

With immune dysfunction known to occur in MND, one such biomarker candidate is neopterin, a marker of cell mediated immune response which is secreted in urine<sup>3</sup>.

We aimed to determine if:

1. Urinary neopterin differs between people with MND and healthy individuals
2. First neurologist visit urinary neopterin levels can be prognostic
3. Longitudinal urinary neopterin levels change with disease

METHODS

- People recruited from SALHN MND Clinic, Adelaide
- Urinary neopterin measured with a Tecan REF9321 ELISA
- Urinary p75<sup>ECDD</sup> measured with an in-house automated ELISA
- Urine and clinical biomarkers

COHORT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MND (n=30)</th>
<th>HI (n=26)</th>
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<tbody>
<tr>
<td>Gender</td>
<td>13 Female, 26 Male</td>
<td>13 Female, 13 Male</td>
</tr>
<tr>
<td>Symptom onset age</td>
<td>66.04 (41.51 – 83.18)</td>
<td>N/A</td>
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<tr>
<td>Diagnosis age</td>
<td>67.13 (41.94 – 84.18)</td>
<td>N/A</td>
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<tr>
<td>Baseline age</td>
<td>67.27 (42.03 – 84.41)</td>
<td>60 (28 – 71.52)</td>
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<td>Baseline ALSFRS-R score</td>
<td>41.15 (32 – 46)</td>
<td>N/A</td>
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<tr>
<td>Diagnostic delay (months)</td>
<td>8.87 (3.02 – 33.94)</td>
<td>N/A</td>
</tr>
<tr>
<td>Disease genotype</td>
<td>26 Sporadic, 4 Familial</td>
<td>N/A</td>
</tr>
<tr>
<td>Site of disease onset</td>
<td>18 Limb, 12 Bulbar</td>
<td>N/A</td>
</tr>
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<td>MND: Motor Neuron Disease; HI: Healthy individuals; All values: median (range)</td>
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URINARY NEOPTERIN IS INCREASED IN MND & CORRELATES TO URINARY P75<sup>ECDD</sup>

- Urinary neopterin levels change throughout disease progression within individual people with MND (n=7). Overall, longitudinal levels are not correlated to time from first neurologist visit (A) but are correlated to time from diagnosis, which is more indicative of disease timeline (B) (Linear regressions).

CONCLUSIONS & NEXT STEPS

Urinary neopterin: Is increased in people with MND
Shows promise as a prognostic biomarker at first neurologist visit
Changes in disease course in individuals

Ongoing work includes more longitudinal measurements to determine if neopterin is useful to subgroup people with MND based on immune status, and if combined urinary neopterin and p75<sup>ECDD</sup> measurement can add value to clinical trial efficacy.

REFERENCES