

**raVO** PNS Line Assays  
for the  
**BlueDiver Instrument**

**PNS9 Diver**  
**PNS11 Diver**



The **rawo** PNS9 DIVER for the detection of the well characterized autoantibodies anti-HuD, anti-Yo, anti-Ri, anti-CV2/CRMP5, anti-Amphiphysin, anti-Ma1, anti-Ma2, anti-SOX1 and anti-GAD65 has been improved by the addition of **Tr- (DNER-)** and **Zic4**. Although both autoantibodies are very rarely detected they play an important role to confine a paraneoplastic etiology in so far unexplained neurological diseases.

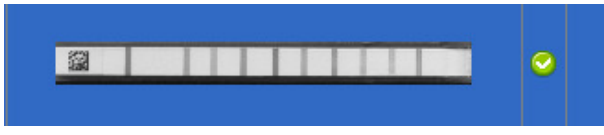
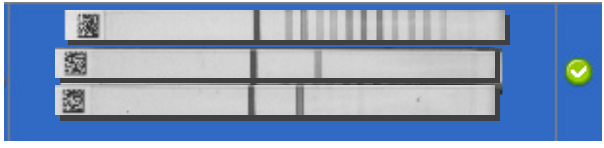
**Tr (DNER):** Autoantibodies to the so-called Tr antigen associated with Hodgkin Lymphoma are known as marker for a paraneoplastic subacute cerebellar degeneration. So far these autoantibodies have been identified by IFA by their typical staining pattern of Purkinje cells. Recently it has been shown that DNER (Delta/Notch-like Epidermal Growth Factor-Related Receptor) is the underlying Tr antigen (1).

**Zic4:** Autoantibodies to Zic4 are associated with paraneoplastic cerebellar degeneration and the underlying tumor is often a small cell lung cancer. Antibodies to HuD and CV2 (CRMP5) and to lesser extent to Ri are also detected in patients with paraneoplastic disorders and antibodies to Zic4. The frequency of Zic4 antibodies in SCLC without paraneoplastic disorders is 16% (2).

#### **Advantages of the *rawo* PNS DIVER Assay:**

- Detection of 9 respectively 11 important neurological autoantibodies on one strip using one serum dilution
- Serum sample dilution 1:140
- Testing of cerebrospinal fluid
- Fully automated test performance
- No cross contamination between samples
- Barcode identification of strips and cartridges
- Automatic reading of results

**Table:**

|   | <b>Paraneoplastic neurological syndromes</b>   | <b>Most frequently associated tumors</b>   |
|---|--|--|
| <b>Anti-Hu-Antibodies</b><br>(ANNA-1)         | <b>Sensory and autonomic neuropathy</b><br><b>Cerebellar ataxia</b><br><b>Encephalomyelitis</b><br><b>Limbic Encephalitis</b>  | Small-cell-lung cancer<br>Non-small-cell lung cancer<br>Extrapulmonary small cell cancer |
| Anti-Yo-Antibodies<br>(Purkinje-cell-antigen) | <b>Cerebellar ataxia</b>   | Breast cancer<br>Ovarian cancer<br>Uterus cancer   |
| Anti-Ri-Antibodies<br>(ANNA-2, anti-Nova-1)   | <b>Brainstem encephalitis</b><br><b>(incl. Opsoclonus-Myoclonus-Syndrome)</b><br><b>Cerebellar ataxia</b>  | Breast cancer<br>Small-cell-lung cancer<br>Medullary carcinoma of the thyroid gland      |
| Anti-CV2-(CRMP5-)Antibodies                   | <b>Sensory and sensorimotor neuropathy</b><br><b>Encephalomyelitis</b><br><b>Cerebellar ataxia</b><br><b>Limbic Encephalitis</b><br><b>Autonomic neuropathy</b><br><b>Chorea</b> | Small-cell-lung cancer<br>Thymom   |
| Anti-Amphiphysin-Antibodies                   | <b>Stiff-person-syndrom</b><br><b>Various symptoms</b>   | Breast cancer<br>Small-cell-lung cancer  |
| Anti-Ma1 and Anti-Ma2- (Ta-) Antibodies       | <b>Limbic Encephalitis</b><br><b>Brainstem encephalitis</b><br><b>Cerebellar ataxia</b>  | Testicular cancer<br>Lung-cancers  |
| Anti-SOX1-Antibodies                          | <b>Lambert Eaton Myasthenia gravis</b>   | Small-cell-lung cancer   |
| Anti-GAD65-Antibodies                         | <b>Stiff-Person-Syndrom</b><br><b>Limbic Encephalitis</b>  | Non paraneoplastic   |
| PNS9 DIVER                                    |    |  |
| Anti-Tr (DNER)-Antibodies                     | <b>Cerebellar truncal and limb ataxia</b>  | Hodgkin Lymphoma   |
| Anti-Zic4-Antibodies                          | <b>Cerebellar degeneration</b>   | Small-cell-lung cancer   |
| PNS11 DIVER                                   |    | Tr (DNER)<br>Zic4  |

**References:**

1. Esther de Graaff, Peter Maat, Esther Hulsenboom, Robert van den Berg, Martin van den Bent, Jeroen Demmers, Pieternella J. Lugtenburg, Casper C. Hoogenraad and Peter Sillescu-Smith. Identification of Delta/Notch-like Epidermal Growth Factor-Related Receptor as the Tr Antigen in Paraneoplastic Cerebellar Degeneration. ANN NEUROL 2012;71:815-824
2. L. Bataller, D.F. Wade, F. Graus, H.D. Stacy, M.R. Rosenfeld, J. Dalmau. Antibodies to Zic4 in paraneoplastic neurologic disorders and small-cell lung cancer. Neurology 2004;62:778-782