NEUROLOGY

# ATN Profile

The first simple, objective blood test to identify Alzheimer's pathology so you can give patients and families clearer answers and take action sooner.

Labcorp's ATN Profile (484400) follows years of blood biomarker research and a guidelines-based clinical framework established by international experts.

## What is ATN?

The ATN framework establishes a means for classifying biomarkers based on the biological evidence of Alzheimer's disease that each marker provides (1). These markers are divided into three categories to reflect the three primary biological changes associated with Alzheimer's:

- **A for amyloid plaques**: Accumulations of beta-amyloid 42 proteins begin to form plaques in the brain years before initial symptom onset
- **T for tau tangles**: The beta-amyloid 42 accumulation causes misfolding of tau proteins, which tangle into knots and disrupt normal brain cell function
- **N for neurodegeneration**: Brain cell functional impairment causes the cells to die, which exacerbates the characteristic cognitive impairment symptoms observed in Alzheimer's patients

| Category | | |
|---|---|---|
| **A** | Beta-Amyloid 42/40 Ratio | Assess levels of pathologic change consistent with Alzheimer's disease |
| **T** | Phosphorylated Tau 181 (pTau181) | |
| **N** | Neurofilament Light Chain (NfL) | Assess disease severity by measuring neurodegeneration |

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## What do the test results mean?

Each ATN biomarker has a cutoff that indicates whether a patient's measured value is consistent with what is observed in amyloid PET positive Alzheimer's patients. For NfL, cutoffs are based on age ranges, as baseline measurable NfL levels increase with age (2,3). Each of the biomarkers is then given an indicator corresponding to consistent with (+) or not consistent with (-) Alzheimer's disease, respectively. This results in eight possible combinations of results, which align to three possible clinical scenarios: normal, AD continuum and non-AD dementia or neurodegenerative condition.

| Profile | Clinical Summary | |
|---|---|---|
| **A- T- N-** | A normal beta-amyloid 42/40 ratio and normal concentrations of pTau181 and NfL were observed at this time. These results are not consistent with the presence of Alzheimer's-related pathology. Plasma findings may be less precise than CSF or PET. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A+ T- N-** | A low beta-amyloid 42/40 ratio was observed. Normal concentrations of pTau181 and NfL were observed at this time. These results may be consistent with the presence of Alzheimer's-related pathology. Plasma findings may be less precise than CSF or PET. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | AD Continuum |
| **A+ T+ N-** | A low beta-amyloid 42/40 ratio and a high pTau181 concentration were observed. A normal NfL concentration was observed at this time. These results are consistent with the presence of Alzheimer's-related pathology. Plasma findings may be less precise than CSF or PET. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A+ T+ N+** | A low beta-amyloid 42/40 ratio and a high pTau181 and NfL concentrations were observed at this time. These results are consistent with the presence of Alzheimer's-related pathology. Plasma findings may be less precise than CSF or PET. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A+ T- N+** | A low beta-amyloid 42/40 ratio and a high NfL concentration were observed. A normal pTau181 concentration was observed at this time. These results may be consistent with the presence of Alzheimer's-related pathology and concomitant suspected non-AD pathological change. Plasma findings may be less precise than CSF or PET. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A- T+ N-** | A high pTau181 concentration was observed. A normal beta-amyloid 42/40 ratio and normal concentration of NfL were observed at this time. These results are not consistent with the presence of Alzheimer's-related pathology, but may indicate pathology of another condition. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A- T+ N+** | High pTau181 and NfL concentrations were observed. A normal beta-amyloid 42/40 ratio was observed at this time. These results are not consistent with the presence of Alzheimer's-related pathology, but may indicate pathology of another condition. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |
| **A- T- N+** | A high NfL concentration was observed. A normal beta-amyloid 42/40 ratio and normal pTau181 concentration were observed at this time. These results are not consistent with the presence of Alzheimer's-related pathology, but may indicate pathology of another condition. Additional assessments may be necessary. These tests are intended to be used only in the context of clinical care. | |

## Does the ATN Profile diagnose Alzheimer's disease?

Biological confirmation of disease is necessary for diagnosis. This test provides evidence of the biological changes that are consistent with Alzheimer's disease. However, Alzheimer's still requires a clinical diagnosis based on clinical observation and cognitive testing.

## How accurate is the test?

The ATN Profile was clinically validated using 200 samples from a well-studied cohort in which all samples were characterized with patient age, sex, amyloid PET status, and clinical diagnosis. The beta-amyloid 42/40 ratio assay showed a ROC analysis area under the curve (AUC) of 0.944, with a sensitivity of 96% and specificity of 86.7%.


**References**

1. Jack, CR, et.al. (2016). A/T/N: An unbiased descriptive classification scheme for Alzheimer disease biomarkers. Neurology, 87(5), 539-547.
2. Hviid, C. V. B., Knudsen, C. S., & Parkner, T. (2020). Reference interval and preanalytical properties of serum neurofilament light chain in Scandinavian adults. Scandinavian journal of clinical and laboratory investigation, 80(4), 291-295.
3. Khalil, M, et.al. (2020). Serum neurofilament light levels in normal aging and their association with morphologic brain changes. Nature communications, 11(1), 812.


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