

## Mapping the Tau Cascade

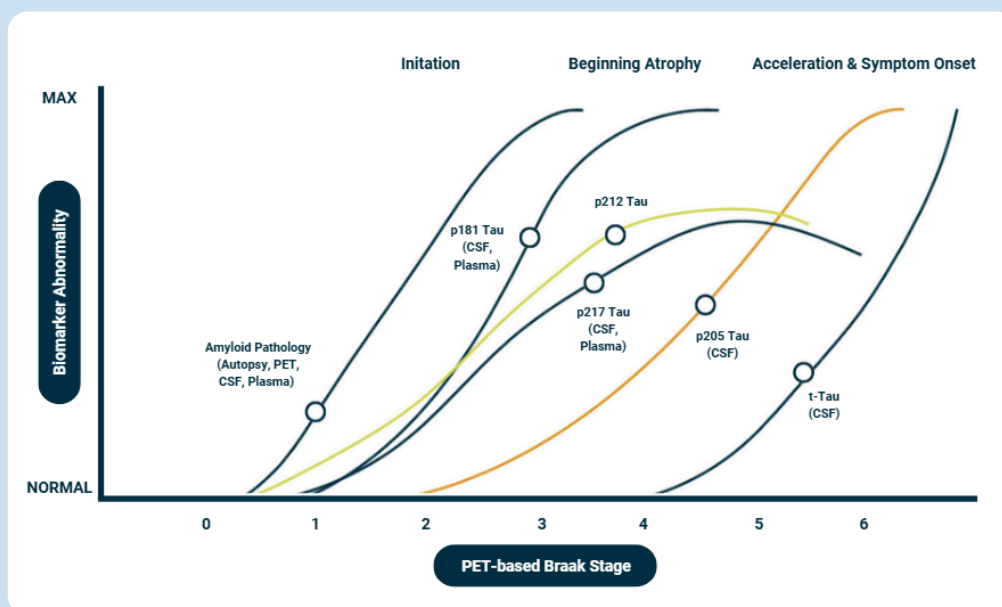
### New Insights from p-Tau 205 and p-Tau 212 for Disease Staging and Monitoring

#### Tau Pathology from Early Dysregulation to Advanced Neurodegeneration

Tau pathology unfolds through a cascade of phosphorylation, aggregation, and regional spread, each stage offering a critical lens into disease biology and therapeutic vulnerability. While p-Tau 181 and p-Tau 217 have anchored early detection and amyloid-associated changes, novel phosphorylation sites, p-Tau 205 and p-Tau 212, extend this framework into later-stage tangle formation and early conformational dysregulation, respectively. These biomarkers represent distinct molecular events: p-Tau 212 emerges during early misfolding of soluble tau, whereas p-Tau 205 aligns with pathogenic tau accumulation and neurodegeneration.

These next-generation markers enable researchers to access deeper mechanistic and temporal insights:

- p-Tau 181 detects early amyloid-induced tau phosphorylation and is widely used for screening and diagnostic enrichment.
- p-Tau 217 improves staging accuracy by correlating with both amyloid and tau PET signals in early to mid-stage progression.
- p-Tau 212 increases early, tracking soluble conformational tau species before clinical decline.
- p-Tau 205 peaks with neurofibrillary tangle formation and cognitive deterioration.
- *Total tau reflects global tau burden and is useful for differentiating Alzheimer's from non-AD tauopathies.*



**Figure 1.** The evolving biomarker landscape in parallel with disease biology. Together, these markers refine our ability to stage pathology, align biomarker strategy to therapeutic mechanism, and monitor Alzheimer's progression with greater fidelity.



Now available from Quanterix, p-Tau 205 and p-Tau 212 assays offer sub-femtomolar sensitivity via Simoa® technology, measurable in CSF, plasma, and serum. Integrating these assays enables a continuous, phase-specific understanding of tau dysregulation.

## Enabling Therapeutic Discovery and Response Monitoring

The expanded tau biomarker portfolio supports therapeutic development strategies from early detection through late-stage intervention.

- p-Tau 205 is especially well-suited for evaluating tau aggregation inhibitors and tracking downstream tangle resolution.
- p-Tau 212 offers a pharmacodynamic lens into earlier intervention points, particularly for therapies targeting soluble tau species.

Together, they can provide powerful tools for:

- Trial enrichment based on stage-specific tau pathology
- Monitoring on-target effects of tau-directed therapies
- Enabling regulatory alignment through objective, molecular endpoints

These assays support a precision medicine framework for clinical research and are optimized for both discovery and translational applications.

## Translational Use Cases

- Trial Optimization: Enrich cohorts based on tau stage specificity
- Mechanistic Insight: Differentiate early conformational shifts from late tangle pathology
- Scalable Monitoring: Measure both markers across CSF, plasma, and serum
- Regulatory Readiness: Incorporate into endpoint selection and filing strategies

## Why Simoa® Matters

Our tau assays are built on Quanterix's ultra-sensitive Simoa platform, delivering:

- Sub-femtomolar detection of phosphorylated tau
- High specificity with minimal background
- Reproducibility across matrices and study sites

## Available Now on the Simoa HD-X Analyzer® Platform

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