Optical tweezers-assisted dynamic force spectroscopy (DFS) is employed to investigate specific receptor/ligand bindings on the level of single binding events. Here, the specific binding of two anti-human tau monoclonal antibodies (mAbs), HPT-110 and HPT-104, to synthetic tau-peptides with different phosphorylation pattern is analyzed (Fig.a). The specificity of HPT-110 to the tau-peptide containing a phosphorylation at Ser235 and of HPT-104 to the tau-peptide containing a phosphorylation at Thr231 is confirmed. Additionally, our approach allows for a detailed characterization of the unspecific interactions that are observed between HPT-104 and the peptide phosphorylated only at Ser235 and between HPT-110 and the peptide phosphorylated only at Thr231. By analyzing the measured rupture-force distributions it is possible to separate unspecific from specific interactions. Thereby for the latter characteristic parameters like the lifetime of the bond without force $\tau_0$, the characteristic length $x_{ts}$ and the free energy of activation $\Delta G$ are determined (Fig.b). The results are in accordance with conventional ELISA tests but offer a much more refined insight [1].

Fig. a: A typical force-distance dependence is shown. The beads are brought in contact and pulled apart with a preset velocity. Due to an individual binding between the tau-peptide and the mAb the particle in the optical trap is shifted out of the equilibrium position. Inset: The experimental configuration. Fig. b: The lifetime of the interaction between HPT-110 and the double-phosphorylated peptide is shown in dependence on the force for 6 different loading rates. Inset: Histogram of the measured rupture forces at a loading rate of 77 pN/s.