

# Evaluation of Creatine Deposits In TgCRND8 Mouse Brain Tissue By Synchrotron Ftir Spectromicroscopy

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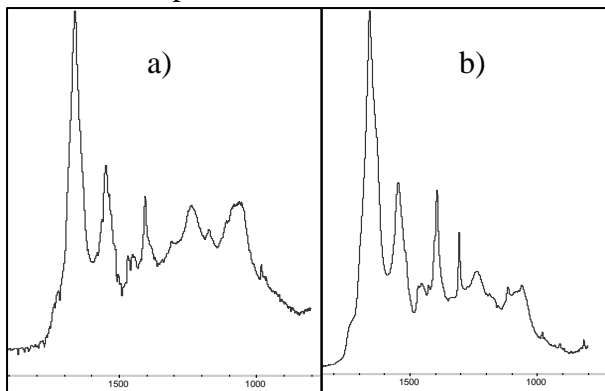
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The creatine-phosphocreatine system plays an important role in energy balance in the brain and is known to be affected in Alzheimer Disease brain. Recently, focally elevated deposits of creatine have been found in the hippocampus of mice expressing doubly mutant (K670N/M671L and V717F) amyloid precursor protein, sacrificed at 34-89 weeks.<sup>1-3</sup> These deposits are larger and significantly greater in quantity in mutant mice than in their littermate controls. The deposits have been further studied in sections of caudal tissue using synchrotron FTIR spectromicroscopy. The goals are (1) to evaluate the distribution of creatine in other brain regions, such as the caudate, between TgCRND8 and littermate control and (2) to map the creatine deposits in serial sections. Deposits of creatine were found in several places in the caudate regions of the TgCRND8 examined. Creatine was also found in the caudate of non-transgenic mice, but these deposits were smaller and much fewer in number than those of the corresponding transgenic mice. Examination of creatine in serial sections of caudate of a 61-week-old transgenic mouse revealed no depth to the creatine deposits.

To date, we had analyzed for creatine using the 1304 cm<sup>-1</sup> peak, as it is usually very distinct from surrounding tissue. However, we observed that sometimes this peak is very small while the 1405 cm<sup>-1</sup> peak is very sharp. In the spectrum of pure creatine (Figure 1), the 1405 cm<sup>-1</sup> peak is part of a doublet, with the second peak at a lower frequency of 1392 cm<sup>-1</sup>. In most cases, both peaks are visible and the 1304 cm<sup>-1</sup> peak is also strong. However, when only the 1405 cm<sup>-1</sup> peak appears, the 1304 cm<sup>-1</sup> peak is very weak, although other peaks characteristic of creatine still appear, confirming that these deposits are indeed creatine. One consequence of this discovery is that analysis for solely the 1304 cm<sup>-1</sup> peak is likely insufficient to visualize all the creatine present in a tissue sample; processing maps for both the 1304 cm<sup>-1</sup> peak and the 1405 cm<sup>-1</sup> peak gives a more complete picture. We hypothesize that this phenomenon is due to creatine deposits of different orientations interacting in the different ways with the polarized light of the synchrotron.



**Figure 1:** Spectra of creatine crystals found *in situ* in TgCRND8 mouse brain, oriented (a) parallel (b) perpendicular to incident beam.

## References:

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