

Interaction of Lens Low Molecular Weight Peptides: Changes in Oligomeric Organization of α B-crystallin

There is an increased cleavage of proteins during aging and cataractogenesis in the lens of the human eye. The protein fragments are known to interact with intact lens proteins. Understanding the interaction of protein fragments with intact crystallins will shed light on the mechanism of protein aggregation *in vivo*.

α B-crystallin is one of the major structural proteins of the lens, with an oligomeric mass of 400–800kDa. Besides its structural role, it is known to *suppress* the aggregation of destabilized proteins, a property suggested to be important for maintaining the lens transparency. We have isolated two peptides of < 3 kDa from an 80-year old human lens water insoluble fraction and tested their interaction with intact recombinant α B-crystallin.

The peptides were incubated with α B-crystallin (1:1 molar ratio) at 37°C. After 4 hours the samples were briefly centrifuged and the supernatant was injected onto a TSK G5000PWXL (Tosoh Bioscience) column fitted to an HPLC with a Shimadzu RI and Wyatt DAWN+QELS detectors. Absolute molar mass, polydispersity and the hydrodynamic radii of the samples were determined using the ASTRA software.

Figure 1 shows the mass distribution across the peak of α B-crystallin incubated with and without peptide A. More than 50% of the α B-crystallin precipitated on interaction with peptide A and that which stayed in solution had a 5–6 fold *increase* in molar mass when compared to an untreated α B-crystallin. Interaction of peptide B did *not* cause α B-crystallin to precipitate, though an increase in molar mass across the α B peak (Figure 2) was observed. Both peptides altered the hydrodynamic radius of α B-crystallin (Table 1).

Our study shows that the interaction of low molecular peptides *changes* the dynamics of α B-crystallin and can induce protein aggregation. The interaction of peptides with proteins may be a key event in diseases like Alzheimer's, Parkinson's and cataracts.

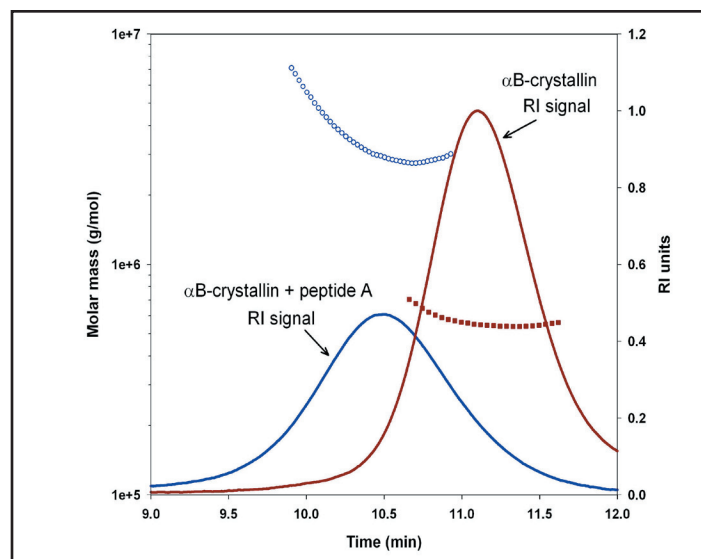


Figure 1. Molar mass distribution of α B-crystallin incubated with (blue circle) and without (brown square) low molecular weight peptide A.

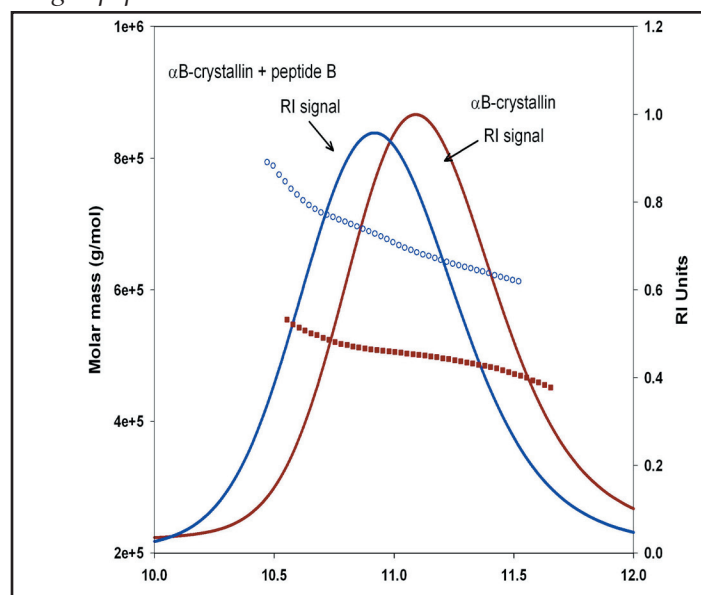


Figure 2. Molar mass distribution of α B-crystallin incubated with (blue circle) and without (brown square) low molecular weight peptide B.

This note graciously submitted by Puttur Santhoshkumar, Padmanabha Udupa and K. Krishna Sharma, Mason Eye Institute, University of Missouri, Columbia, MO.

	Mass in peak(g)	Mass distribution peak (g/mol)	M_w avg. (g/mol)	PDI	Hydrodynamic radius(nm)
Experiment 1					
α B-crystallin	3.20e-5	7.04e+5 – 5.58e+5	5.72e+5 (0.1%)	1.003 (0.9%)	8.1 (3%)
α B-crystallin + peptide A	1.77e-5	7.13e+6 – 2.98e+6	3.23e+6 (0.1%)	1.056 (2%)	15.9 (0.4%)
Experiment 2					
α B-crystallin	1.14e-4	5.53e+5 – 4.57e+5	5.06e+5 (0.1%)	1.001 (0.9%)	7.5 (0.5%)
α B-crystallin + peptide B	1.15e-4	9.45e+5 – 6.14e+5	7.03e+5 (0.1%)	1.006 (2%)	8.3 (0.5%)