PA1, a Proteasomal Catalytic Activator, is a Protective Agent Against Oxidative Stress Including the Prevention of Protein Aggregation

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Efficient proteolysis of damaged proteins is determinant for maintenance of cellular homeostasis. The ubiquitin-proteasome system is responsible for the degradation of the majority of intracellular protein. Our group has been performing the screening of proteasomal modulators. One of the compounds isolated, termed Proteasomal Activator 1 (PA1), is an important catalytic activator responsible for 30 – 85% (10-100 µM) proteasomal activation when incubated with cellular models. Since there are very few proteasomal activators described so far, the goal of present work was to examine PA1 role in the cellular protection against oxidative stress. This possibility is based on solid reports in the literature showing that oxidized proteins are preferentially degraded by the catalytic unit of the proteasome complex by a process not dependent on protein ubiquitinylation. Moreover, oxidation is a widespread protein modification, intensified through aging and underlying pathogenesis of some degenerative diseases, *e.g.* neurodegeneration. Results obtained thus far revealed that cells incubated in the presence of PA1 and challenged with hydrogen peroxide showed decreased pool of either oxidized or aggregated proteins and neither loss of cell viability nor alteration in the pool of poly-ubiquitinylated proteins. These results are relevant because show that the incubation with PA1 does not promote apparent modification of cellular homeostasis, considering that the pool of ubiquitinylated proteins was unaltered, and preserved viability of cells challenged with hydrogen peroxide. Next steps will be to test PA1 effects on life span in an appropriated cellular model.