Prions and cancer: A story unfolding

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Prions, the causal agents of Mad Cow and other diseases, are very unique infectious particles. They are proteins in which the complex molecular three-dimensional folding process just went astray. For reasons not yet understood, the misfolding nature of prions is associated to their ability to sequester their normal counterparts and induce them to also adopt a misfolding conformation. The ever-growing crowd of misfolded proteins form the aggregates seen in diseases such as Parkinson's and Alzheimer's. Once misfolded, a protein can no longer exert its normal functions in the cell.

Now, a group led by Dr Jerson Lima Silva at the Federal University of Rio de Janeiro, Brazil, presents some new evidence that p53, a protein with the daunting task of suppressing tumor formation in the body, may show a typical prion-like behavior when mutated.

It has been known for some time that the buildup of p53 in the cell impairs the protein in preventing tumor growth. This has been observed in neuroblastoma, retinoblastoma, breast, and colon cancers. In a paper entitled "Mutant p53 aggregates into prion-like amyloid oligomers and fibrils: Implications for cancer" and published in the *Journal of Biological Chemistry*, the group shows that in breast cancer cell lines carrying the most common p53 mutation, the formation of amyloid-like aggregates of p53 proteins may explain the protein's lack of function.

Whether this prionoid behavior in fact represents a relevant cancer-related mechanism remains to be shown. Development of novel and ingenious strategies to prevent p53 misfolding and aggregation may be

just one way to find out.

"We are planning pre-clinical tests with synthesized nucleic acids in an attempt to prevent the changing in conformation of normal p53, and avoid aggregates of misfolded protein," says Dr. Silva.

If successful, the strategy may help unveil unforeseen molecular mechanisms leading to tumor development. Considering that more than half of the cancers lose p53 function, this prionoid behavior may serve as a potential novel target for cancer therapy, dramatically transforming our way of thinking of cancer and treating cancer patients.

More information: *Journal of Biological Chemistry* doi: 10.1074/jbc.M112.340638