Reducing drug allergies without compromising efficacy

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An enzyme that usually triggers strong allergic reactions now circulates in the veins of a group of mice without alerting the immune system. As INRS Énergie Matériaux Télécommunications Research Centre Professor Marc A. Gauthier explains in an article published in the journal *Nature Communications*, a polymer was used to camouflage the enzyme before it was injected into the rodents. This was achieved by coating the enzyme to avoid an immune response in a manner that does not compromise its activity. The first in vivo demonstration has opened the door to numerous clinical applications.

The strategy proposed by Professor Gauthier and his Swiss co-investigators solves a very real problem. Molecules with high therapeutic potential sometimes degrade rapidly in the bloodstream or cause allergies. This is the case for an enzyme used to fight lymphoblastic leukemia, L-asparaginase, that causes allergies in nearly 20% of patients.

The research team used a comb-shaped polymer (poly-OEGMA*) that covers the enzyme like a fur coat. Antibodies are unable to attach to the protected enzyme: L-asparaginase combined with poly-OEGMA is 3,000 times less recognizable by antibodies than "naked" L-asparaginase.

"Generally speaking, when other cutting-edge approaches in the field are used, enzymes are efficiently protected but lose a significant amount of their activity," said Gauthier. "We are the first to show, in vivo, that comb-shaped polymers are much better at protecting enzymes than other approaches, since they reduce enzyme activity only slightly."

For the approach to work, the molecules that the enzyme transforms must be small enough to slide between the polymer "hairs." Otherwise, the reaction cannot take place. In the case of L-asparaginase, the efficacy of the approach is now proven and it can be tested on other similar enzymes.

Furthermore, poly-OEGMA could protect other therapeutic molecules that are rapidly degraded, by preventing them from making contact with the proteins that inactivate or break them. This other application is equally promising.

More information: The article published in *Nature Communications* is entitled "Semi-permeable coatings fabricated from comb-polymers efficiently protect proteins in vivo." DOI: 10.1038/ncomms6526

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