

Theranostic Iminoglyco-NPs targeting the Blood Brain Barrier

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Gaucher's disease (GD) is a rare autosomal recessive disease caused by a deficiency in the activity of the glucocerebrosidase (GCase) enzyme due to mutations in the GBA gene. Studies show that GBA genetic mutations are also a risk factor for Parkinson's disease, suggesting that therapeutic approaches to modulate GCase activity could play an important role in treating both diseases [1]. An innovative therapeutic strategy for the treatment of GD is the use of pharmacological chaperones (PCs) to enhance natural enzymatic activity, although currently no PC has yet reached the market for this pathology. Iminosugars and other substrate analogues acting as competitive inhibitors of GCase are promising candidates as PCs [2]. As the blood brain barrier (BBB) represents an obstacle for the classical enzyme replacement treatment of neuronopathic forms of GD, the synthesis of novel iminosugars functionalized with specific ligands able to enhance the transport through the BBB is being investigated. In addition, since a greater affinity between enzyme and multivalent iminosugars has been demonstrated, the multimerization of the iminosugars onto nanoparticles (NPs) will be carried out to combine the properties of the inhibitors to the multivalency of the NPs, thus yielding smart systems with theranostic properties [3].

References

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