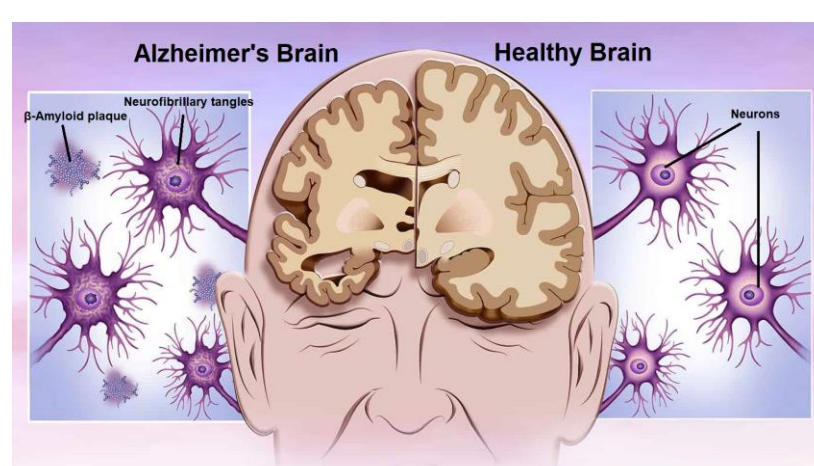
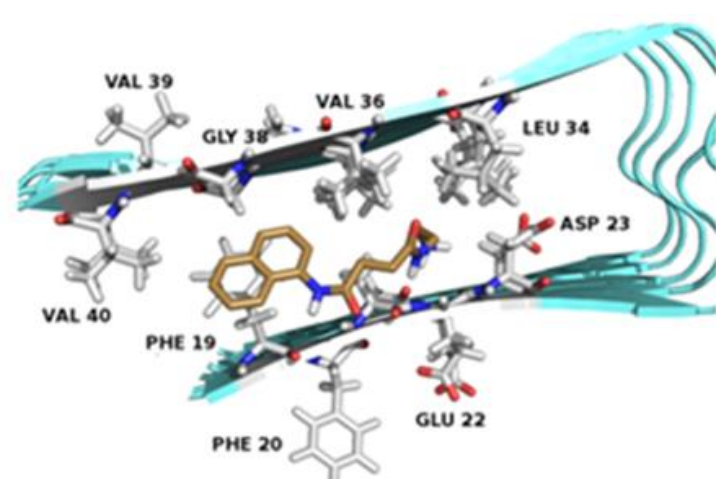


Desing of Gadolinium or Iron based contrast agents for senile plaques detection by MRI

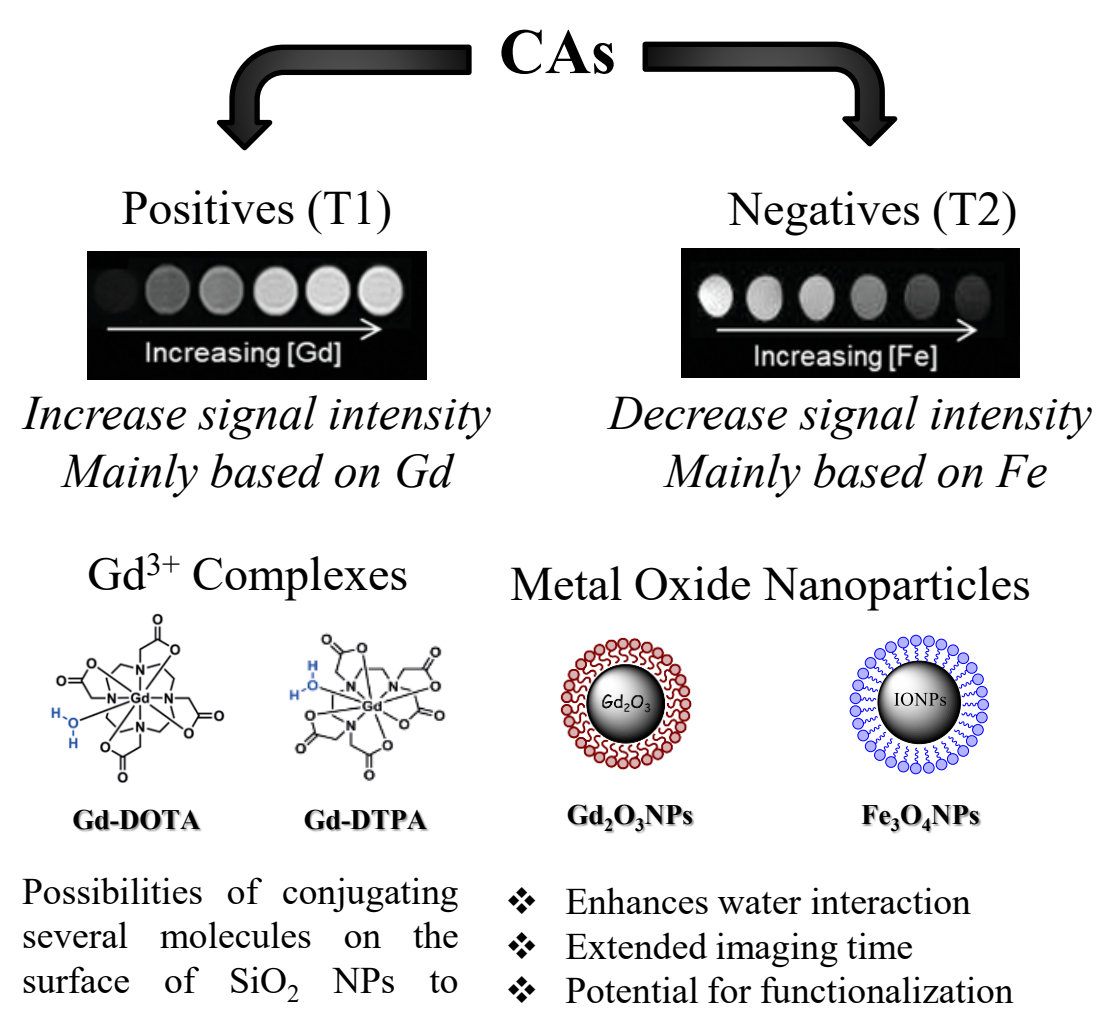
Jeréz C.N.^{1,2}, Guerrero G.R.^{1,2,3}, Becker A.², Le Calvé S.², Kiefer C.⁴, Rodríguez Ch.¹, Díaz A.³, Mertz D.⁴, Sablón M.¹, Begin S.²¹Cuban Center for Neuroscience, Biocubafarma, Havana, Cuba²Institute of Chemistry and Processes for Energy, the Enviroment and Health (UMR 7515 CNRS), University of Strasbourg, Strasbourg, France³Bioinorganic Laboratory, Faculty of Chemistry, University of Havana, Havana, Cuba⁴Institute Physical and Chemistry Materials of Strasbourg, (UMR 7504 CNRS), University of Strasbourg, Strasbourg, France

INTRODUCTION & AIM

Histopathology of Alzheimer's disease (AD)

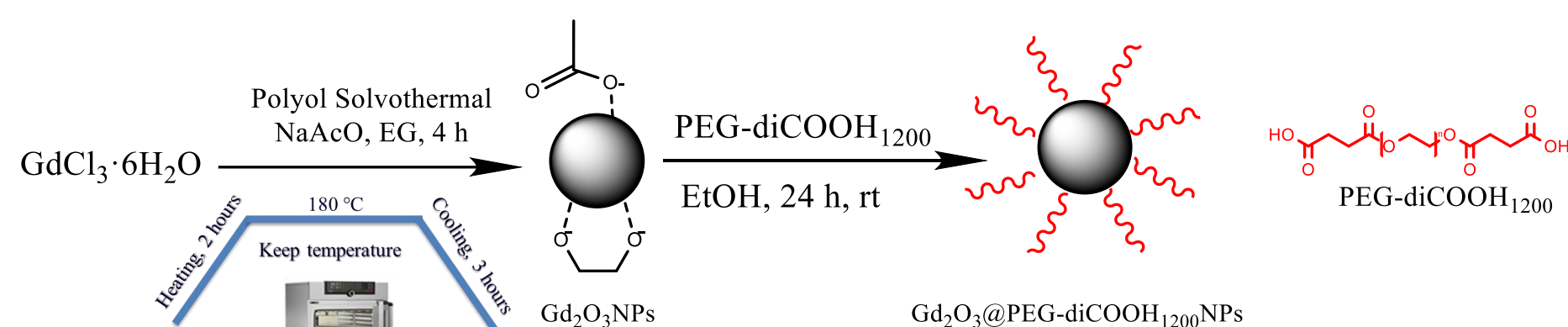
Amylovis: targeting ligand for β -Amyloid ($A\beta$) plaquesInteraction zone between β -fibrils and Amylovis[®] between the a.a. from 12 to 26 (VHHQKLFFAEDVGS) [5]

Types of contrast agents (CAs) for MRI

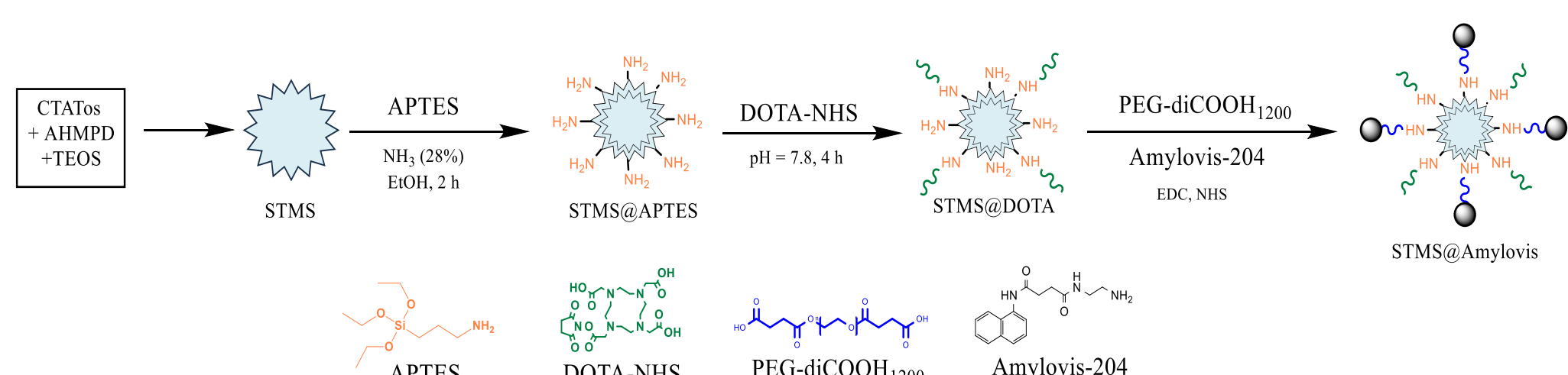


This work describes the synthesis of two types of CAs: positive or T1 (gadolinium oxide nanoparticles (Gd_2O_3 NPs) or metal complexes supported on silica nanoparticles (SiO_2 NPs)) and negative or T2 (iron oxide nanoparticles (IONPs)). These CAs are functionalized with Amylovis compounds as target ligands (TLs) related to βA in order to design smart probes for the specific diagnosis of AD using MRI.

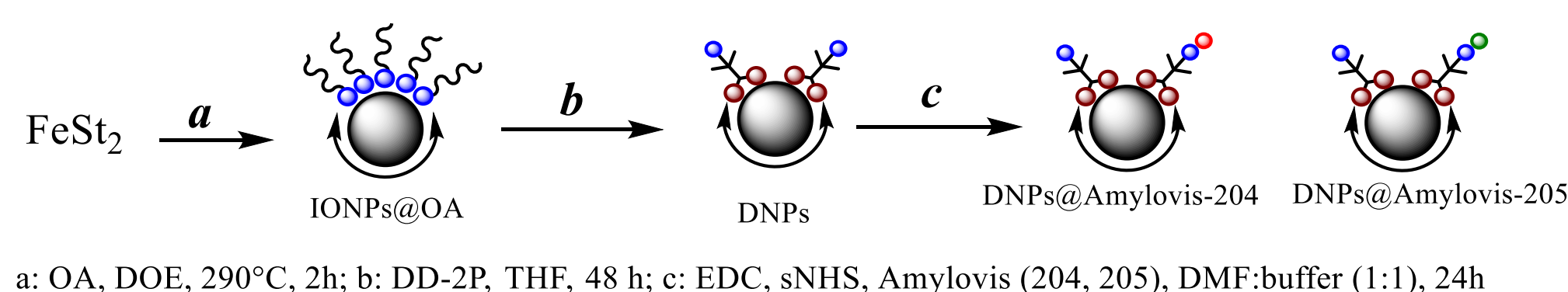
METHOD

Synthesis of $Gd_2O_3@PEG-diCOOH_{1200}$ 

Synthesis of STMS@DOTA@Amylovis



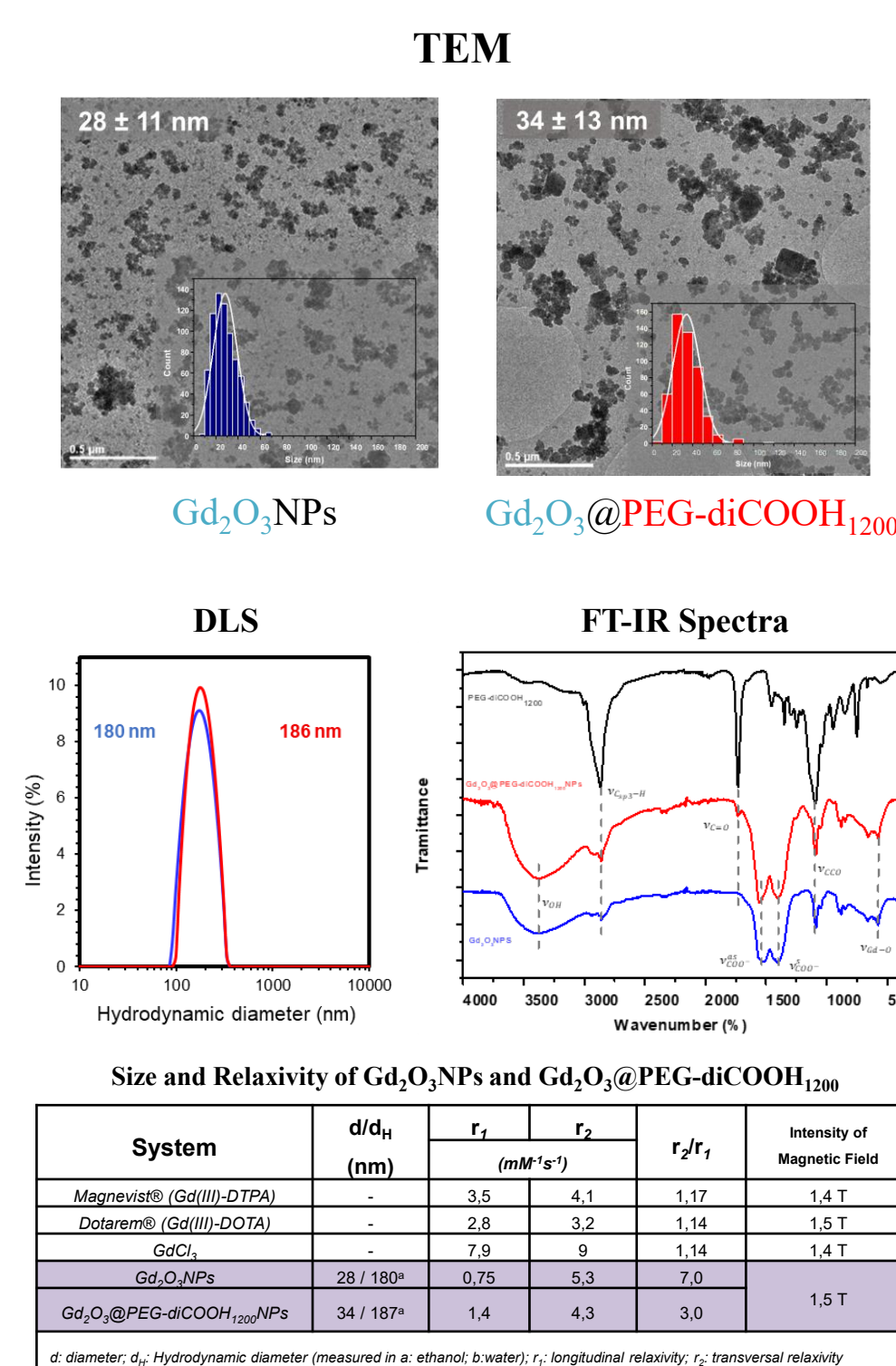
Synthesis of DNPs@Amylovis



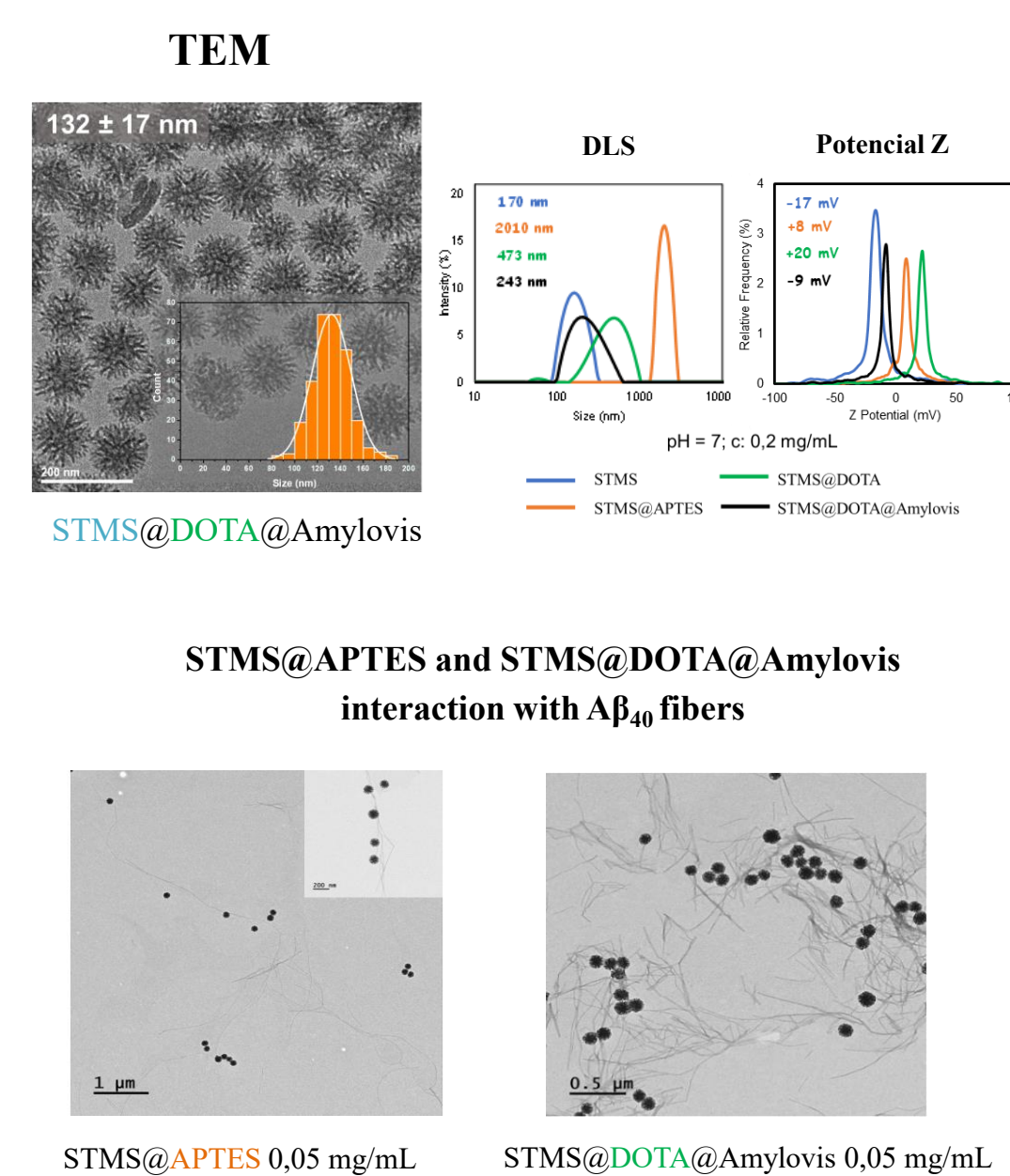
a: OA, DOE, 290°C, 2h; b: DD-2P, THF, 48 h; c: EDC, sNHS, Amylovis (204, 205), DMF:buffer (1:1), 24h

ACKNOWLEDGEMENTS

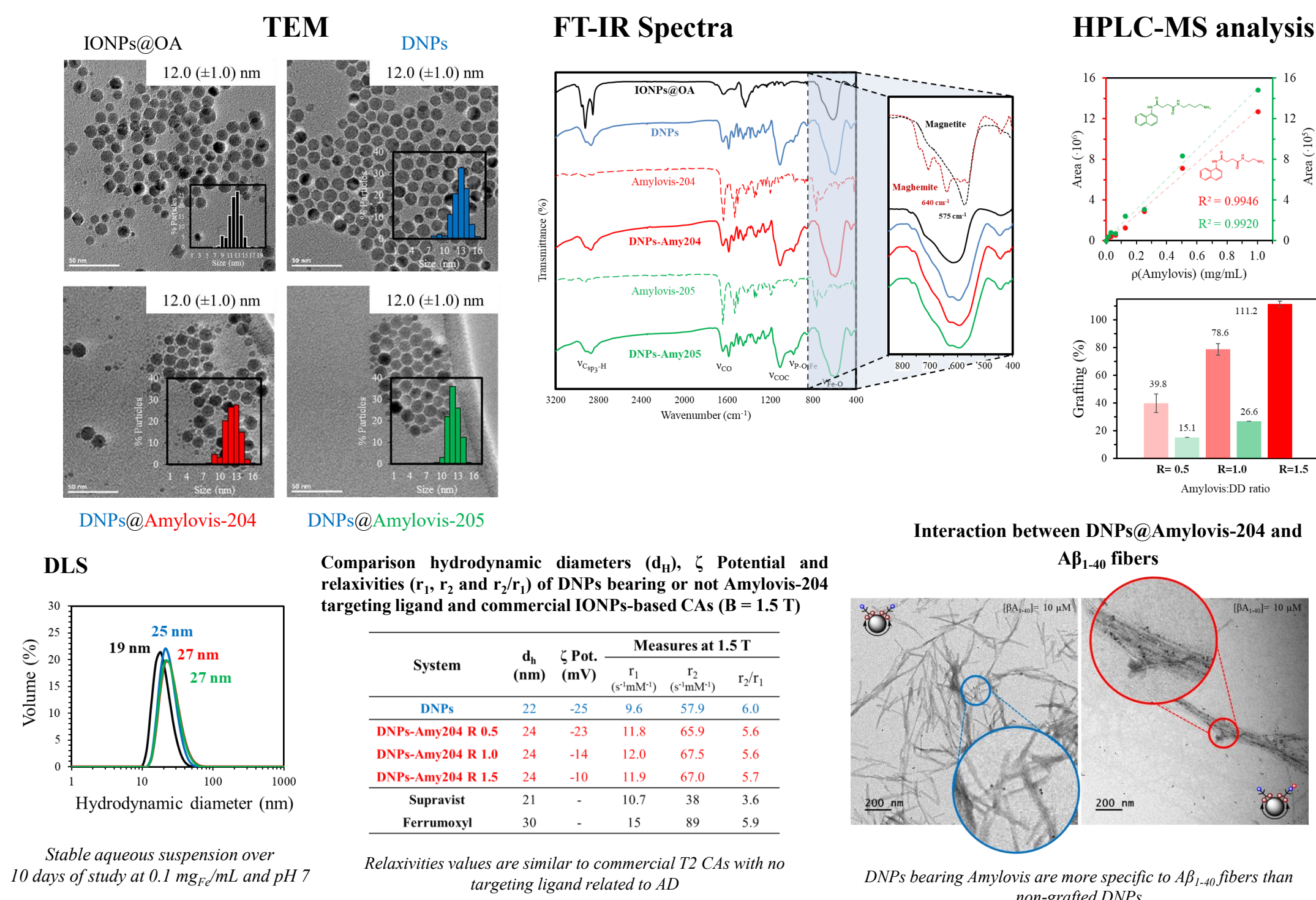
RESULTS & DISCUSSION

Synthesis of $Gd_2O_3@PEG-diCOOH_{1200}$ 

Synthesis of STMS@DOTA@Amylovis

Although both systems bind to $A\beta_{40}$ fibers, the particles functionalized with Amylovis demonstrate a higher affinity

Synthesis of DNPs@Amylovis

Stable aqueous suspension over 10 days of study at 0.1 mg_p/mL and pH 7

Relaxivities values are similar to commercial T2 CAs with no targeting ligand related to AD

DNPs bearing Amylovis are more specific to $A\beta_{1-40}$ fibers than non-grafted DNPs

CONCLUSION

Two types of Amylovis-functionalized metal nanoparticles (metal-complexed SiO_2 and IONPs) were successfully synthesized. For $Gd_2O_3@PEG-diCOOH_{1200}$, functionalization was not possible, as it requires a higher surface density of $PEG-diCOOH_{1200}$ to prevent aggregation. Their surface functionalization and nanometric sizes (all under 200 nm) were confirmed. This work successfully lays the groundwork for developing targeted MRI contrast agents to improve the detection of senile plaques in Alzheimer's disease.

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