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Surface supported dynamic combinatorial chemistry for biomacromolecule recognition

Miao, Xiaoming

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Samenvatting

In dit proefschrift wordt de selectieve chemische functionalisering van nanomaterialen onderzocht, gebaseerd op dynamisch covalente chemie (DCC). Dit proefschrift is verdeeld in drie hoofdstukken, die achtereenvolgens de bereiding van nanodeeltjes verspreid in water (hoofdstuk 2), de dynamische hydrazonuitwisseling aan het oppervlak van dendrimeren (hoofdstuk 3) en de specifieke functionalisering van dendrimeren door dynamische imine chemie (hoofdstuk 4) behandelen.

In hoofdstuk 2 zijn SPIONs met zwitterionische liganden gesynthetiseerd, die over een lange periode (> 60 dagen) stabiel bleven in waterige oplossing. Een op choline fosfaat gebaseerd zwitterionisch ligand met een aldehyde groep maakte het mogelijk om het oppervlak te functionaliseren door middel van hydrazonchemie, wat de mogelijkheden van SPIONs laat zien als een nieuw platform voor DCC aan een oppervlak.

In hoofdstuk 3 hebben we reversibele hydrazonchemie op zwitterionische PAMAM dendrimeren laten zien. Het uitwisselingsgedrag en het thermodynamische evenwicht is eerst geverifieerd door middel van NMR en UPLC, waarna het toevoegen van drie DNA oligonucleotide templates leidde tot vermenigvuldiging van de onderdelen van de bibliotheek met de hoogste affiniteit voor deze DNA templates. Eén positief geladen hydrazon op het oppervlak van PAMAM liet een bijzonder sterke vermenigvuldiging zien, waarschijnlijk dankzij zijn vermogen om te binden met het negatief geladen DNA.

In hoofdstuk 4 hebben we dynamische iminechemie laten zien op het oppervlak van zwitterionische dendrimeren. Verschillende enkele en dubbele DNA oligonucleotiden zijn gebruikt als templates om de oppervlaktefunctionalisering van de dendrimeren te sturen. De schaal van de synthese van drie DCLs, blootgesteld aan de verschillende DNA templates, is vergroot om de dendrimeer te kunnen isoleren en de bindingsaffiniteit vast te stellen middels ITC. Deze bindingsstudies tonen aan dat de bibliotheken mét templates een sterkere bindingsaffiniteit en specificiteit hadden dan de bibliotheken zonder templates. Dit illustreert dat DCC een makkelijke en efficiënte methode is om specifieke receptoren te genereren die DNA binden, in één geval zelfs sequentie-selectief. Meer diepgaande onderzoeken in de toekomst zullen moeten uitwijzen in hoeverre een aanpak gebaseerd op DCC in staat is DNA of peptideketens op een meer

Samenvatting

sequentie-specifieke manier te onderscheiden. Een selectievere methode zou kunnen leiden tot opwindende toepassingen, zoals de specifieke herkenning van een verzameling biologische of medische targets.

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