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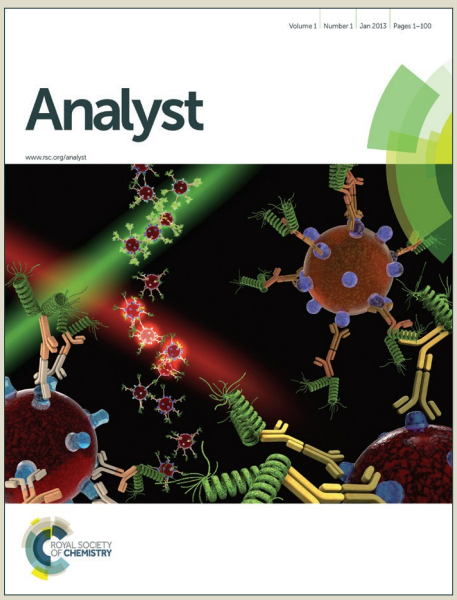

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PAPER

Specific G-quadruplex structure recognition of human telomeric RNA over DNA by fluorescently activated hyperporphyrin†

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Human telomeric repeat-containing RNA (TERRA), that has recently been found to play an important role in living cell as its DNA counterpart, solely adopts a parallel G-quadruplex (G4) topology. However, developing a highly selective fluorescence probe specific for the TERRA G4 is a great challenge, since difficulty arises in differentiating it from the DNA G4s that possess polymorphism structures including parallel, (3+1) hybrid, basket, and chair topologies. In this work, 5,10,15,20-tetrakis(3,5-dihydroxyphenyl)porphyrin (TOH_dPP) was selected out from various porphyrins as the most efficient fluorescence probe in targeting TERRA. We found that only the TERRA binding is effective in activating the TOH_dPP's hyperporphyrin spectra, favoring red-shifted spectral bands and enhanced fluorescence emission. Following the previous investigations on the TERRA G4 structure and our present experiments, we anticipate that TOH_dPP most likely interact with the 5' tetrads of two TERRA G4s via a 1:2 sandwich association. Since the ribose 2'-OH favors the loop adenine residue-extended tetrad G4 plane that is only specific for TERRA, thus besides π-stacking with the G4 tetrads, TOH_dPP should also interact with this substructure to trigger an efficient electron communication between the tetraphenyl substituents and the porphyrin macrocycle, as required by the hyperporphyrin effect. The hydrogen bonding interactions of the eight hydroxyl substituents in TOH_dPP with the backbone phosphate oxygen atoms of TERRA most likely further contribute to the binding selectivity. Our work demonstrates the potential of TOH_dPP as the selective TERRA G4 fluorescence probe and a promising TERRA-based sensor reporter.

Introduction

Following more insights into the structure, recognition and biological importance of human telomeric DNA G-quadruplex (DNA G4), human telomeric repeat-containing RNA (TERRA) has been recently acquired to be transcribed by the telomeric DNA in mammalian cells.[1,2] TERRA has been anticipated to involve in the process of telomere shortening and elongation and could serve as a biomarker for identification of telomere-related cancer development.[3-6] Therefore, it is expected that small molecules that can specifically associate with TERRA can ideally serve as therapeutic agents for effectively tuning this biological process.[7]

Different from the DNA counterparts possessing global polymorphic G4 structures with parallel, (3+1) hybrid, basket, and chair topologies that are highly dependent on the involved sequences and existing environments,[8,9] TERRA with various lengths solely adopts a parallel G4 structure (TERRA G4) in diluted solution[10-17] and even in living cells.[18-20] The TERRA G4 parallel topology is less sensitive to the existing environments and even in Na^+ solution it adopts a similar structure as in K^+ solution.[13-17] Additionally, the TERRA G4 is more thermo-stable than the DNA counterpart.[16,21,22] Along with having thoroughly elucidated the TERRA G4 structure, there exists an open challenge to find fluorescent ligands that can selectively target such parallel G4 structure against the DNA G4 counterpart possessing varieties of parallel, basket, hybrid, and chair structures.[8,9,23] On the other hand, these selective ligands also have promising applications in using TERRA G4 as the sensor element due to its less structure diversity and more stability in comparison with the DNA counterpart.

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† Electronic Supplementary Information (ESI) available: Experimental procedures, oligonucleotides used in this work, structure of investigated porphyrins, excitation and emission spectra of TOH_dPP in the presence of TAG4, excitation and emission spectra of PPIX in the presence of PS2.M, rUAG4, and TAG4, absorption spectra of TOH_dPP in acidic solution, effect of Mg^{2+} on the fluorescence intensity, and TERRA melting temperatures. See DOI: 10.1039/x0xx00000x

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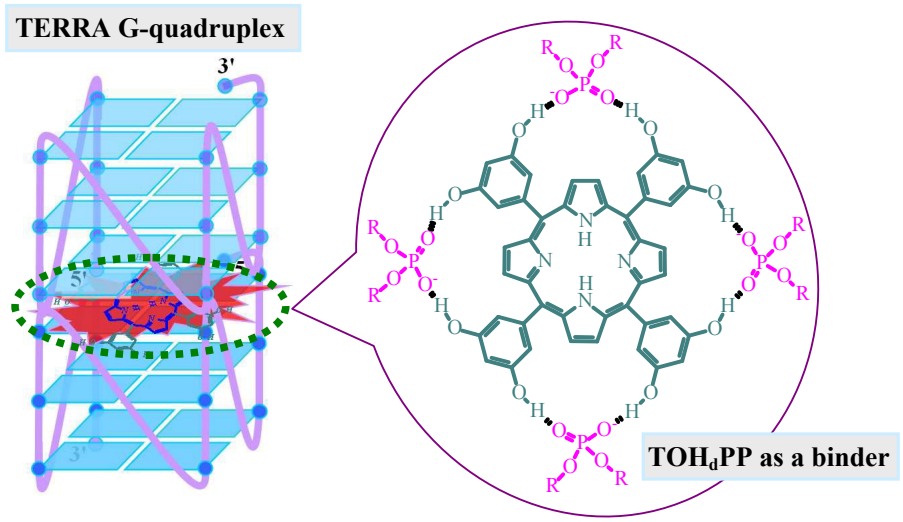

Scheme 1 The proposed binding model of TOH_dPP with TERRA G4. Besides the hydrogen bonding interaction of TOH_dPP with TERRA phosphate backbone, additional hydrogen bonding interaction of TOH_dPP with the 2'-OH and C3'-endo[22] of the ribose near the binding site should also include in the binding. This interaction pattern was omitted for clarity. In comparison with the other porphyrins, this TERRA interaction is only specific for TOH_dPP and most likely contributes to the observed selectivity.

The pyrene-labeled excimer and fluorochrome-labeled antibody have been used for investigating the TERRA structure.[18,20] As for the label-free methods, chemicals of chelerythrine,[24] PyroTASQ,[25] carboxypyridostatin,[26] fluorinated fragment,[27] acridine,[28,29] and BRACO-19/naphthalene diimide[30] have been employed to target TERRA G4 by fluorescence and other techniques. But these probes suffer from a lower binding affinity[27] and the high selectivity for the TERRA G4 over the DNA G4[24-26,30] has yet to be further explored. Furthermore, in comparison with the fruitful reports of DNA G4 recognition using various fluorescent probes,[29,31] much less effort has been made for the TERRA G4 fluorescence recognition due to the inherent difficulty in structure differentiation from the DNA G4.[24,25]

Porphyrins contain a multiple electron-conjugated macrocycle and subsequently give very intense absorption and fluorescence bands in the visible region. Due to the similar π electron character with the tetrad of G4, porphyrins have long been used as fluorescent probes for DNA G4 targeting via π-π stacking interaction, especially those possessing various periphery substituents of negatively charged groups (protoporphyrin IX, [32] N-methyl mesoporphyrin IX [33 - 36]), positively charged groups (substituted at the meso position with quaternary pyridinium[37-40] and others[41,42]), and metalated derivatives.[43 -46] Although some of these probes are successful in recognizing certain DNA G4 structures, no effort has been made in finding an appropriate porphyrin for selectively targeting the TERRA G4 by fluorescence. In this work, 5,10,15,20-tetrakis(3,5-dihydroxyphenyl) porphyrin (TOH_dPP) is screened out as the selective TERRA G4 emitter. TOH_dPP is a hyperporphyrin [47] possessing multiple hydroxyl groups. Hyperporphyrin exhibits characteristically spectroscopic features different from the classical Gouterman π-π* model expectation as a results of charge transfer (CT) between the peripheral substituents and the porphyrin macrocycle. In solution, the tetraphenyl substituents at the macrocycle meso-carbon positions have orientation that not favors the CT process with the porphyrin macrocycle.[48,49] It is expected that TOH_dPP would exhibit hyperporphyrin effect when the phenyl substituents have a good electron communication with the porphyrin macrocycle.[49] Our work demonstrates occurrence of the TOH_dPP hyperporphyrin property upon specifically binding with the TERRA G4, suggesting a high recognition selectivity in both emission wavelength and intensity over the DNA G4. On

our point of view, this is the first report on the TERRA G4/nucleic acid fluorescence recognition using activated hyperporphyrin as the selective probe.

Results and discussion

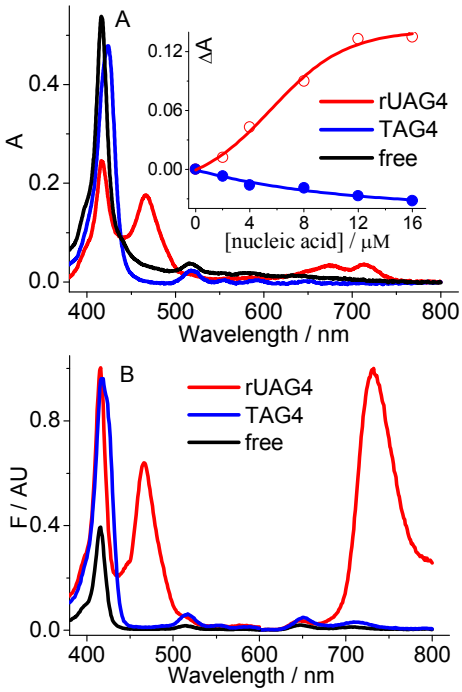

Fig. 1 (A) Absorption spectra of TOH_dPP (4 μM) in 0.1 M K^+ in the absence (black line) and presence of 16 μM rUAG4 (red line) or TAG4 (blue line). Inset: Absorbance changes at 467 nm after addition of nucleic acids. (B) Excitation and emission spectra of TOH_dPP (4 μM) in 0.1 M K^+ in the absence (black line) and presence of 4 μM rUAG4 (red line) or TAG4 (blue line). λex = 467 nm; λem = 732 nm.

TOH_dPP as an efficient hyperporphyrin in selectively targeting TERRA G4 over the other DNA G4 structures by a switch-on fluorescence response

We first investigated TOH_dPP binding to the rUAG4 TERRA having 5'-UA-3' residue at the 5' tetrad end in comparison to its DNA counterpart (TAG4, Table S1) due to their specific structure preferences (parallel[10,15] versus hybrid[8] in K^+ solution). As shown in Fig. 1A, TOH_dPP free in solution gives a strong Soret band at 416 nm and four weak Q bands at 517, 555, 591, 648 nm, representative for poprphyrin absorption bands.[47] A small change in these bands was observed when TAG4 was incubated with TOH_dPP. However, addition of rUAG4 resulted in appearance of a new Soret band at 467 nm and two Q bands at 675 and 713 nm, suggesting the selective affinity of TOH_dPP to the TERRA G4. The Soret band becomes broader and the two substantially red-shifted Q bands exhibit enhanced oscillator strengths, indicating a typical hyperporphyrin effect.[47-49] These extra absorption bands are most likely attributed to π (substituted phenyl)-π* (porphyrin) charge transfer (CT) transition[50] of hyperporphyrin that is favored by TERRA binding. The hyperporphyrin effect can be visible in different concentrations of TOH_dPP (Inset of Fig. 1A). On the other hand, the specific affinity of TOH_dPP to the TERRA G4 structure over the DNA G4 was further verified by fluorescence spectra. The TAG4 binding makes TOH_dPP fluorescently emitting at 646 and 706 nm with a 416 nm excitation band, identical to the TOH_dPP free in solution, although the resulted fluorescence intensity is slightly higher (Fig. S1). However, the rUAG4-bound TOH_dPP shows another fluorescence excitation band at 467 nm and a red-shifted emission band at 732 nm, significantly different from the DNA counterpart TAG4 (Fig. 1B). The fluorescence intensity with the rUAG4 incubation is about 60 times brighter than that with the DNA counterpart TAG4 under 467 nm excitation. The red-shifted emission and enhanced fluorescence also suggest the hyperporphyrin effect.[47-49] Thus, the resultant hyperporphyrin effect makes TOH_dPP as a promising fluorescent probe in recognizing the TERRA G4 by both the specific emission wavelength and intensity significantly different from the DNA G4 binding.

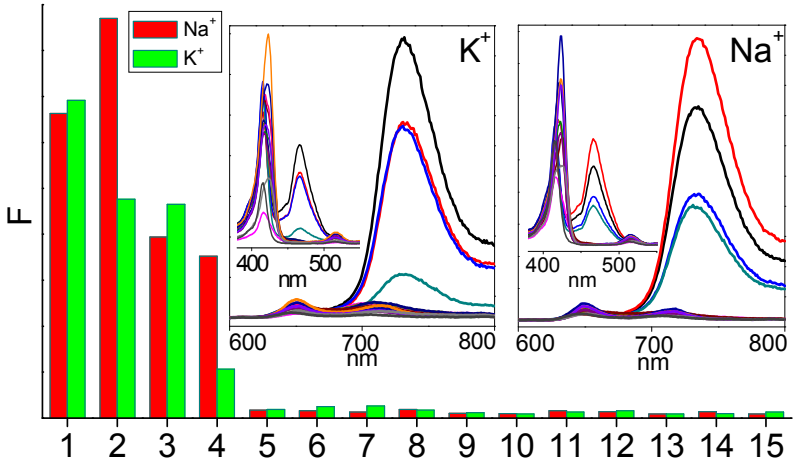

Fig. 2 Dependence of TOH_dPP (4 μM) fluorescence intensity at 732 nm in 0.1 M K^+ and Na^+ solutions on G4 sequences (4 μM). Inset: the corresponding excitation and emission spectra for the G4s. The 732 nm emission bands and 467 nm excitation bands are visible only for TERRA G4s. From 1 to 15 for the G4s: rUAG4 (1), rAG4 (2), rUUAG4 (3), rUUAG4UUA (4), 1XAV (5), T3TT (6), T3TT3 (7), 2O3M (8), TAG4 (9), AG4 (10), TTAG4 (11), TTAG4TTA (12), AG4T (13), TTAG4T (14), and PS2.M (15).

In order to generalize the selective recognition by the hyperporphyrin effect, we also compared the fluorescence responses for the other TERRA G4s possessing various 5' residues (rAG4 and rUUAG4) with their DNA counterparts (AG4 and TTAG4, Table S1). rAG4[17,30] and rUUAG4[13,15] have also been investigated to adopt parallel G4 conformations in K^+ solution. As does rUAG4 *versus* TAG4, the representative hyperporphyrin fluorescence bands arise only for rAG4 and rUUAG4 rather than for AG4 and TTAG4 (Fig. 2). In order to get an insight into the effect of the 3' residue of TERRA on the TOH_dPP fluorescence, a 5'-UUA-3' residue was further added to rUUAG4 at its 3' end to give rUUAG4UUA. In comparison with its DNA counterpart TTAG4TTA, rUUAG4UUA also favors the fluorescence bands resulting from the hyperporphyrin effect. Although the fluorescence intensities are somewhat affected by the 5' and 3' residues of TERRAs (Fig. 2), it is convinced that the hyperporphyrin emission bands appear solely for the TERRA G4s.

It has been reported that the TERRA G4 topology is much less dependent on the solution conditions. For example, TERRA can also form parallel structures in Na^+ solution,[13-17] against the basket topology adopted for the DNA counterpart G4s in Na^+.[8] We also checked the hyperporphyrin preference of TOH_dPP in binding to these Na^+-determined structures. Interestingly, as shown in Fig. 2, all the TERRA G4s activate the hyperporphyrin emission, while the DNA counterparts are as dim as in K^+, again reflecting the parallel TERRA G4-supported binding of TOH_dPP over the basket DNA G4s in the state of hyperporphyrin.

Unlike the human telomeric DNA G4s adopting hybrid and basket conformations in K^+ and Na^+, other potential G4 DNA sequences derived from the oxytricha telomere (T3TT, T3TT3), oncogene c-myc promoter (1XAV), c-kit promoter (2O3M), and a DNAzyme (PS2.M) form parallel, chair, and unresolved G4s in K^+ and Na^+, respectively.[8] Fortunately, these G4s are still unable to light up the hyperporphyrin emission either in K^+ or in Na^+ (Fig. 2). Conclusively, it seems that the TERRA parallel G4 structures are highly specific in converting TOH_dPP to the hyperporphyrin state, which is strongly unfavorable for varieties of the DNA G4s, even those with a parallel topology.

The TERRA-activated hyperporphyrin fluorescence was further investigated using various porphyrins including PPIX, ZnPPIX, MPIX, NMPPIX, TCPP, TOHPP, TM_dPP, and TBr_dPP as probes (Scheme S1). It has been reported that PPIX can target parallel G4 structures with an enhanced fluorescence response,[32] while ZnPPIX suffers from a poor G4 structure selectivity.[51] According to our prediction, PPIX, ZnPPIX, MPIX, and NMPPIX should exhibit no hyperporphyrin emission because the electron-donating peripheral substituents in these porphyrins are absent and thus can't provide the improved electronic communication of their substituents with the porphyrin macrocycle after binding with G4s. This is confirmed by the observations of no 732 nm emission for these porphyrins (Fig. 3, with rUAG4, 1XAV, and TAG4 serving as representatives of TERRA, DNA parallel, and DNA hybrid G4 structures, respectively). As a further example, PPIX indeed experiences a fluorescence increase when binding with PS2.M (Fig. S2), as observed in a previous report,[32] but suffers from a much smaller shift in excitation and emission bands. Furthermore, PPIX in the presence of rUAG4 emits at the wavelength similar to the PS2.M G4 (Fig. S2). Thus, it is inefficient in discriminating TERRA from the DNA G4s.

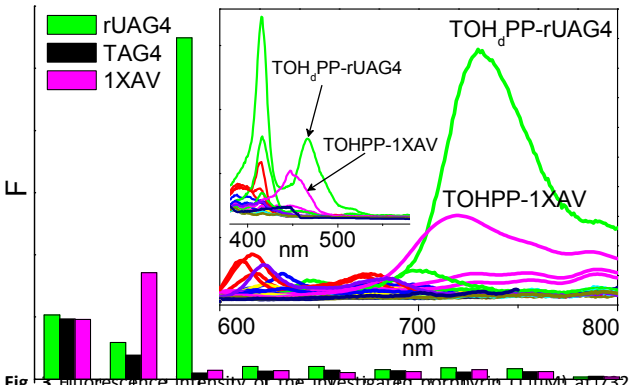

Fig. 3 Fluorescence intensity of the investigated porphyrin (1 μM) at 732 nm (excitation at 467 nm) in 0.1 M K^+ in the presence of rUAG4 (red), TAG4 (black), and 1XAV (green) (1 μM). From 1 to 9 for porphyrins: TCPP (1), TOHPP (2), TOH_dPP (3), PPIX (4), ZnPPIX (5), MPIX (6), NMPPIX (7), TM_dPP (8), and TBr_dPP (9). Inset: the corresponding excitation and emission spectra for the porphyrin-G4s. The nucleic acid-TCPP spectra were omitted for clarity because no changes were found in comparison with TCPP free in solution.

We then checked TCPP, TOHPP, TM_dPP, and TBr_dPP that instead possess the same tetraphenyl substituents as TOH_dPP, but have various substituents at their phenyl rings (Scheme S1). Among them, TCPP' fluorescence responses in the presence of rUAG4, 1XAV, and TAG4 are comparable with it alone in solution, suggesting the poor binding with these nucleic acids due to the four negatively charged carboxyl substituents. When TOHPP was used that contains only one hydroxyl substituent at the para-position of each phenyl ring, instead of two hydroxyl substituents at the two meta-positions in TOH_dPP, only 1XAV, but not rUAG4, trigged a small hyperporphyrin emission at 716 nm (Fig. 3). Moreover, further adding two bromide substituents at the two meta-positions of each phenyl ring in TOHPP generates TBr_dPP and none of rUAG4, 1XAV, and TAG4 is effective in activating TBr_dPP's hyperporphyrin emission. Interestingly, for TM_dPP that is derived by

replacement of the eight hydroxyl substituents in TOH_dPP with eight methoxyl groups, the hyperporphyrin emission was totally lost even in the presence rUAG4, although this porphyrin was most likely aggregated in solution. Therefore, the substituents at the phenyl rings in these tetraphenyl porphyrins play an important role in lighting up the hyperporphyrin emission.

Previous reports have revealed that the TERRA G4 exhibits a higher stability than the DNA counterpart.[16,21,22] We carried out the fluorescence experiments for rUAG4 with coexistence of TAG4 and found that the coexistence of the DNA G4 showed no interference on the TOH_dPP's fluorescence response towards the TERRA G4 (Fig. S3). This provides the possibility of selective recognition of the TERRA G4 even in a mixture with the DNA G4 by the TOH_dPP's hyperporphyrin emission.

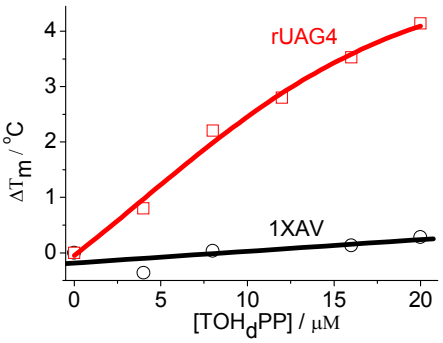

Fig. 4 Change of rUAG4 and 1XAV (4 μM) melting temperature (Tm) with increasing the TOH_dPP concentration. The melting temperatures were obtained in 50 mM Tris-HCl (pH=7.8) containing 20 mM K^+ and 1 mM EDTA.

Analysis of binding mode for the high selective recognition of TERRA over DNA G4s via the TOH_dPP's hyperporphyrin activation

Based on the above experimental results, we can reach a conclusion that TOH_dPP is the most efficient porphyrin in selectively recognizing TERRA over DNA G4s within the investigated porphyrins. This recognition results in red-shifted absorption and emission bands and enhanced fluorescence of TOH_dPP, namely, the hyperporphyrin effect. Such good performance in such recognition event with massive changes in both emission wavelength and intensity suggests that TOH_dPP can serve as a promising candidate in fluorescently probing TERRA G4 structure and developing TERRA-based sensors. The poor TOH_dPP fluorescence responses for the DNA G4s most likely reflect its low affinity to these nucleic acids, as confirmed by the small change in the DNA melting temperature upon adding TOH_dPP (using parallel 1XAV as a typical example, Fig. 4). However, the increasing in the TERRA melting temperature (using parallel rUAG4 as a typical example, Fig. 4) again emphasizes the π-π binding-trigged spectral changes for the RNA G4s. However, the π-π interaction between the tetrad of the TERRA G4 and the porphyrin macrocycle should not be the only driving force in contributing to the recognition event, since all the investigated porphyrins could work with this interaction mode. Thus, the TOH_dPP interaction should strongly rely on the specific TERRA structure that is instead inoperative for the DNA G4s.

It has been reported that TERRA has the propensity to self-associate in solution via the tetrad contacts of 5'-5', 3'-3', and 3'-5',[10,12,13,16] maybe dependent on the residue sequences beyond the G-quadruplex. Especially for the 5'-5' self-association, the adenine residues of the propeller-like loops are reoriented within the plane of the 5' tetrad of the TERRA G4, which thus provides the possibility of additional A-A stackings between the two stacked TERRA G4s, besides the 5'-5' tetrad stacking.[10,12,13] Such propensity of self-association complicates assignment of the high resolution structure that is even unresolved by NMR.[16,23] Along with such flexible loop arrangement, these adenine residues are easily involved in interaction with the TERRA ligands.[28,29] Thus, a significant loop conformational change could occur as a result of the ligand binding via the A-extended planar tetrad platform and hydrogen bonding interactions.[28,29] Therefore, the 5' tetrad in TERRA should be the TOH_dPP binding site due to the propensity of self-association through this tetrad, as observed for the hydrophobic acridine ligand.[28] On the basis of this structure feature specific for TERRA G4, TOH_dPP should interact with TERRA G4 according to a 1:2 binding model, as revealed by the Job's plot analysis for rUAG4 with a perfect turning point of 0.34 (Fig. 5A). The two TERRA molecules most likely associate with TOH_dPP via a sandwich association (Scheme 1).[28,29] By stacking of the porphyrin macrocycle and the tetraphenyl substituents in TOH_dPP with the A-extended planar platform in TERRA, the global structure involving the porphyrin macrocycle and the tetraphenyl substituents should become more coplanar. This coplanarity would favor charge transfer (CT) from the tetraphenyl substituents to the porphyrin macrocycle, resulting in the hyperporphyrin effect.[48] Theoretical[52] and experimental[41] investigations have revealed enhanced NIR absorption and emission bands because of the CT transitions. Following this electron communication, the multiple hydroxyl groups in TOH_dPP should also exert somewhat role in hyperporphyrin effect due to their electron-donating properties.[48] The possibility that the TERRA binding-induced protonation[47] of the porphyrin macrocycle could result in the hyperporphyrin effect was ruled out, because the TOH_dPP spectra in acidic solution (Fig. S4) are significantly different from the spectra observed in the presence of the TERRA G4.

Another important factor that should be considered for the TOH_dPP selective affinity is the hydrogen bonding interaction, since there are hydrogen bonding networks[22,28] including a special contribution from the backbone phosphate oxygen atoms and the ribose 2'-OH in TERRA to stabilize the G4 parallel structure. The hydrogen bonding interaction with these groups are believed to partially contribute to the ligand binding with TERRA.[26,30] Additionally, The U residue above the 5' tetrad of TERRA has been found to be also involved in the interaction with ligands via hydrogen bonding.[28] Among all the investigated porphyrins, since TOH_dPP carries eight hydroxyl groups, its hydrogen bonding interaction with the backbone phosphate oxygen atoms and/or the ribose/U residues would

be rather responsible for the binding selectivity. Since Mg^{2+} is more specific in binding with the nucleic acid' backbone phosphate by electrostatic force than with the bases, the Mg^{2+} concentration in the solution was gradually increased to check the role of the backbone phosphate in the TOH_dPP binding. We found that after a prompt increase in fluorescence (most likely as a result of the extraordinary contribution of the divalent ion on the TERRA stability and the sandwich assembly), a relatively sluggish decrease in fluorescence was subsequently followed (Fig. S5), presumably suggesting the involvement of the backbone phosphate oxygen atoms of TERRA in the hydrogen bonding interaction with TOH_dPP (Scheme 1). This hydrogen bonding pattern for TOH_dPP as depicted in Scheme 1 reasonably benifits from less steric hindrance. This interaction force should synergically work with the stacking interaction occurring for the A-extended planar platform in TERRA, which would further strengthen the coplanar topology of the tetraphenyl substituents and the porphyrin macrocycle to favor the hyperporphyrin effect. This type of interaction provides exceptional insights for the design of more efficient TERRA-interacting molecules.

We also carried out fluorescence titration experiments to determine the binding affinity of TOH_dPP with TERRA G4s. As shown in Fig. 5B, the 1:2 binding model is further convinced by the good curve fittings (solid lines with R^2 between 0.992 and 0.998) that give the binding constants of $2.86\pm0.66\times10^6$, $2.81\pm0.48\times10^6$, and $1.12\pm0.32\times10^6$ M^{-1} for rUAG4, UUAG4, and rAG4, respectively. However, the affinity for rUUAG4UUA ($4.05\pm0.71\times10^5$ M^{-1}) is relatively lower, maybe reflecting its exceptional self-association other than the usual 5'-5' contact and different thermo-stability, as revealed by the lower melting temperature for this TERRA G4 (Table S2). In spite of this difference, TOH_dPP can still selectively recognize rUAG4, UUAG4, rAG4, and rUUAG4UUA via the hyperporphyrin effect, in sharp contrast with the too weak such fluorescence responses for the DNA G4s to accurately predict the binding constants (Fig. 5B, using 1XAV and TAG4 as representatives for the parallel and hybrid DNA G4s). The results from the coexistence experiments observed in Fig. S3 also support the poor binding of the DNA G4s with TOH_dPP. Additionally, note that for all the investigated TERRA G4s, TOH_dPP exhibits a two-orders-of-magnitude higher affinity than the previously reported probe.[27]

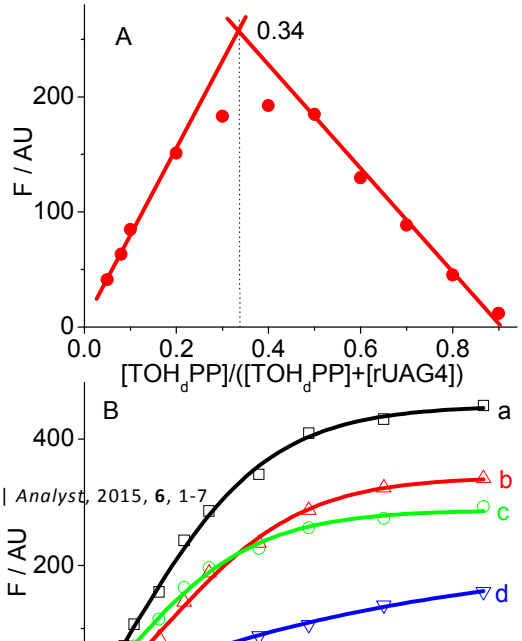

Fig. 5 (A) Job's plot analysis of the stoichiometry of TOH_dPP binding to rUAG4. (B) Dependence of fluorescence intensity of TOH_dPP (1 μM) upon gradually adding G4 into, showing a 1:2 binding model by the curve fitting (solid line): rUAG4 (a), rUUAG4 (b), rAG4 (c), and rUUAG4UUA (d). The solid lines for 1XAV (e) and TAG4 (f) are only for clarity, not the fitting results of the binding mode.

Conclusions

In this work, we developed an efficient fluorescence probe TOH_dPP in targeting TERRA parallel G4 structure. The TERRA binding favors the red-shifted spectral bands and enhanced fluorescence emission of TOH_dPP, which is well known as hyperporphyrin effect. The activated hyperporphyrin emission was not found for the DNA G4s that possess structures including parallel, (3+1) hybrid, basket, and chair topologies, suggesting the high selectivity for TERRA G4 recognition. The fact that among the investigated porphyrins, only TOH_dPP exhibits the hyperporphyrin effect upon binding with TERRA inspired us to propose a binding model. Considering the TERRA structural feature, we believe that TOH_dPP most likely interact with the 5' tetrads of two TERRA G4s via a 1:2 sandwich association. The G4 tetrad, the adenine residues that are coplanar with the tetrad, and the hydrogen bonding interaction with TERRA should be collectively involved in the binding with TOH_dPP. These specific interactions should trigger a coplanar conformation between the tetraphenyl substituents and the porphyrin macrocycle. Thus, the improved CT process between them favors occurrence of the hyperporphyrin effect. Our work develops a first fluorescence probe with a high selectivity for TERRA G4 recognition and proposes the potential of TOH_dPP as a reporter for the future TERRA-based sensors, due to TERRA's higher stability and less structural polymorphism than the DNA G4.

Acknowledgements

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Specific G-quadruplex structure recognition of human telomeric RNA over DNA by fluorescently activated hyperporphyrin

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Selectively recognizing the G-quadruplex structure of human telomeric RNA (TERRA) over DNA was achieved using activated hyperporphyrin as fluorescent probe.