BODIPY-Based Photothermal Agents for Cancer Treatment

Bernhard Spingler[1], Lukas Schneider[1], Martina Kalt[1], Samuel Koch[1], Shanmugi Sithamparanathan[1], Veronika Villiger[1], Johann Mattiat[1], Flavia Kradolfer[1], Ekaterina Slyshkina[1], Sandra Luber[1], Mathias Bonmarin[1], Caroline Maake[1]

[1] University of Zurich, Zurich, Switzerland;
[2] Zurich University of Applied Sciences, Winterthur, Switzerland
spingler@chem.uzh.ch

We will report about novel, easily accessible BODIPY photosensitizer for cancer treatment.[1] In contrast to established photodynamic therapy (PDT) agents [2, 3, 4], these BODIPY-based compounds show photothermal activity and their cytotoxicity is independent of reactive oxygen species (ROS). The agents show high toxicity upon light irradiation and low dark toxicity in different cancer cell lines in 2D culture as well as in 3D multicellular tumour spheroids (MCTSs). The ratio of dark to light toxicity (phototoxic index, PI [5, 6, 7, 8, 9, 10, 11]) of these agents exceeds 830'000 after irradiation with energetically low doses of light at 630 nm. Under hypoxic conditions (0.2% O_2), which are known to limit the efficiency of conventional photosensitizers (PSs) in solid tumours [12], an excellent phototoxic index of 360'000 was observed, indicating a photothermal mechanism of action (MOA). Both phototoxic values are the highest reported to date.

We thank the University of Zurich and the R'Equip programme of the Swiss National Science Foundation (project number 206021_164018) for financial support. L.S. was supported by a UZH Forschungskredit grant (Forschungskredit-Beitrag FK-085-19, co-financed together with the Colbianco Stiftung).

[1] L. Schneider, M. Kalt, S. Koch, S. Sithamparanathan, V. Villiger, J. Mattiat, F. Kradolfer, E. Slyshkina, S. Luber, M. Bonmarin, C. Maake, B. Spingler, manuscript submitted.
[2] R. L. Yanovsky, D. W. Bartenstein, G. S. Rogers, S. J. Isakoff, S. T. Chen, *Photodermatol. Photoimmunol. Photomed.*, **2019**, 35, 295-303.
[3] G. Gunaydin, M. E. Gedik, S. Ayan, *Front. Chem.*, **2021**, 9, 686303.
[4] S. Anand, T. A. Chan, T. Hasan, E. V. Maytin, *Pharmaceuticals*, **2021**, 14, 447.
[5] A. Naik, R. Rubbiani, G. Gasser, B. Spingler, *Angew. Chem. Int. Ed.*, **2014**, 53, 6938-6941.
[6] P. M. Antoni, A. Naik, I. Albert, R. Rubbiani, S. Gupta, P. Ruiz-Sanchez, P. Munikorn, J. M. Mateos, V. Luginbuehl, P. Thamyongkit, U. Ziegler, G. Gasser, G. Jeschke, B. Spingler, *Chem. Eur. J.*, **2015**, 21, 1179-1183.
[7] L. Schneider, M. Larocca, W. Wu, V. Babu, R. Padrutt, E. Slyshkina, C. König, S. Ferrari, B. Spingler, *Photochem. Photobiol. Sci.*, **2019**, 18, 2792-2803.
[8] R. Rubbiani, W. Wu, A. Naik, M. Larocca, L. Schneider, R. Padrutt, V. Babu, C. König, D. Hinger, C. Maake, S. Ferrari, G. Gasser, B. Spingler, *Chem. Commun.*, **2020**, 56, 14373-14376.
[9] N. A. Le, V. Babu, M. Kalt, L. Schneider, F. Schumer, B. Spingler, *J. Med. Chem.*, **2021**, 64, 6792–6801.
[10] R. Padrutt, V. Babu, S. Klingler, M. Kalt, F. Schumer, M. I. Anania, L. Schneider, B. Spingler, *ChemMedChem*, **2021**, 16, 694-701.
[11] L. Schneider, M. Kalt, M. Larocca, V. Babu, B. Spingler, *Inorg. Chem.*, **2021**, 60, 9416–9426.
[12] L. Hong, J. Li, Y. Luo, T. Guo, C. Zhang, S. Ou, Y. Long, Z. Hu, *Biomolecules*, **2022**, 12, 81.