

Nanomedicine and Nanoscale Delivery I

Tomáš Etrych, DSc



INTEGRATING
Delivery Science
ACROSS DISCIPLINES



Polymer theranostics with multiple stimuli-based activations



INSTITUTE OF
MACROMOLECULAR
CHEMISTRY
CZECH ACADEMY OF SCIENCES

Tomáš Etrych, Marina Rodrigues Tavares and Vladimír Šubr,
Institute of Macromolecular Chemistry, Czechia;



Jun Fang,
Sojo University, Japan;

CONTROLLED RELEASE SOCIETY
CRS 2024 Annual Meeting
AND Exposition
JULY 8-12, 2024 • BOLOGNA, ITALY

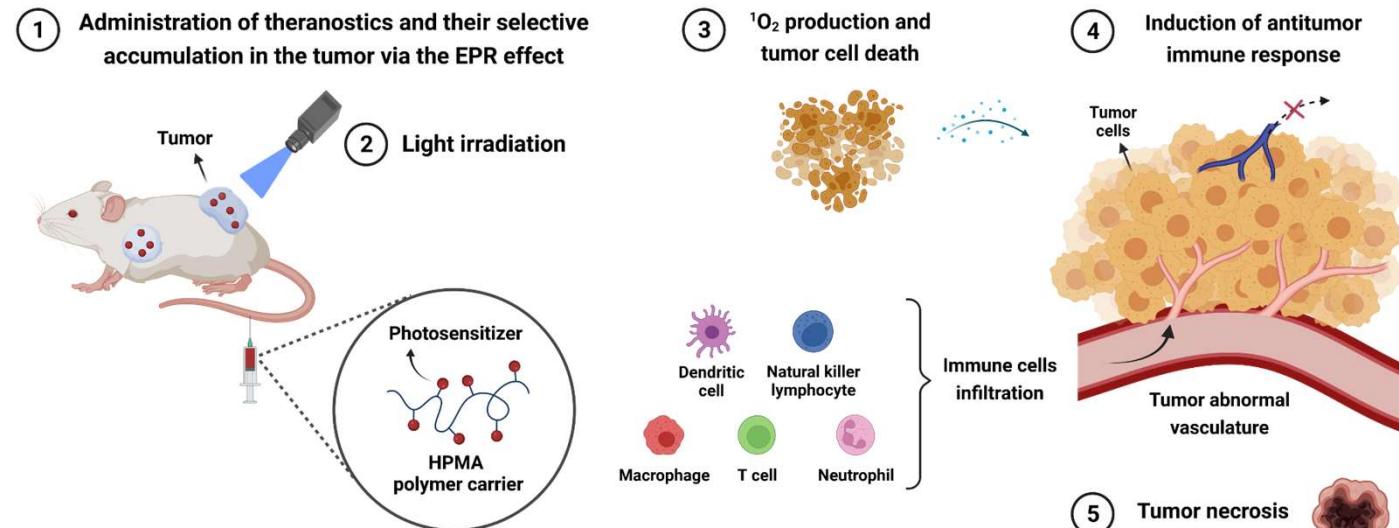
INTEGRATING
Delivery Science
ACROSS DISCIPLINES

NiCR NATIONAL INSTITUTE
FOR CANCER RESEARCH

 Czech Academy
of Sciences

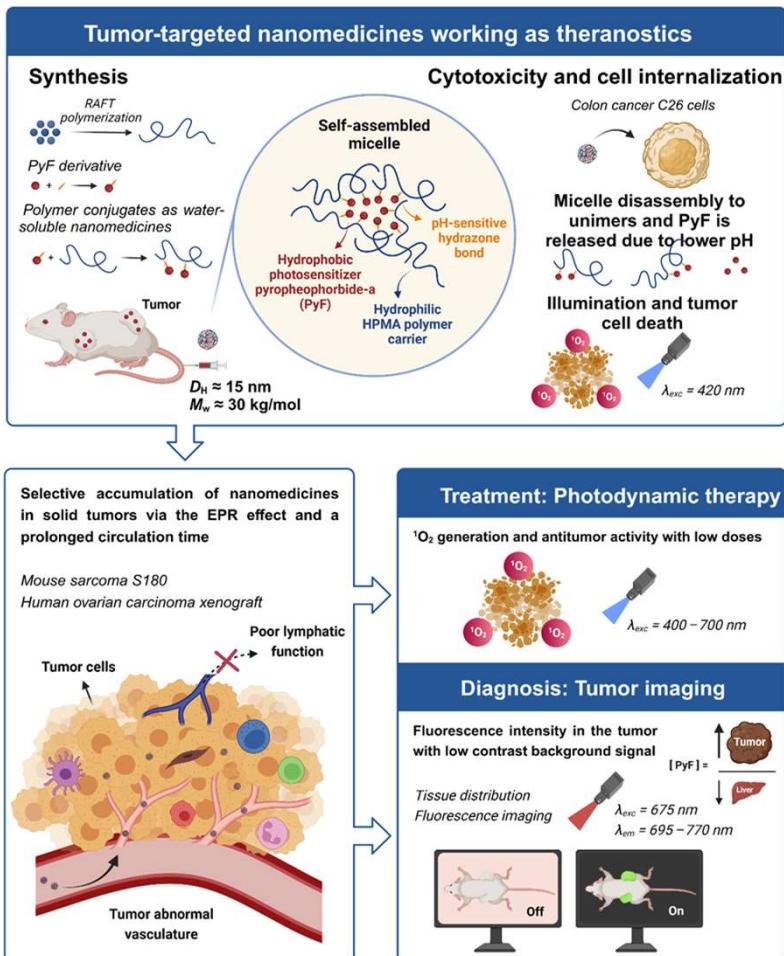


Photodynamic therapy

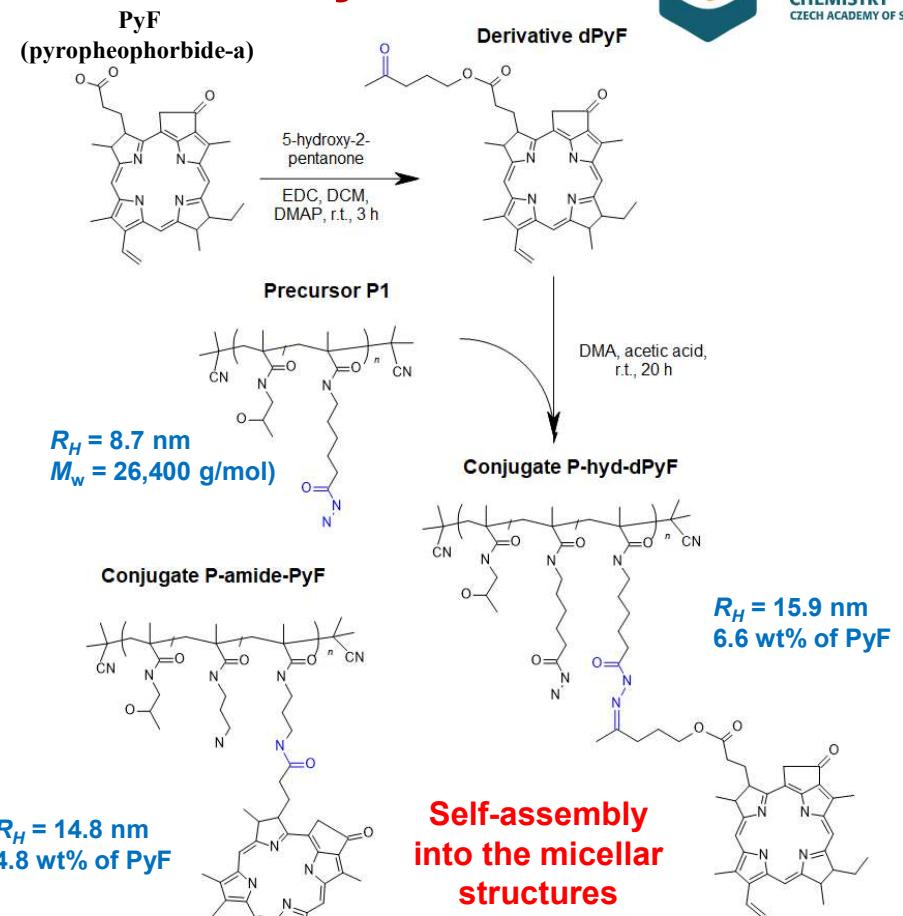


- Principle: photosensitizer strongly absorbs the light, which is then converted to energy and heat in the irradiated areas → production of reactive oxygen radicals, i.e., singlet oxygen species, $^1\text{O}_2$ ($^1\Delta_g$) → cell death;
- Advantages:
 - No long-term side effects;
 - Less invasive than surgery;
 - Unlike radiation, PDT can be repeated many times at the same site if needed.

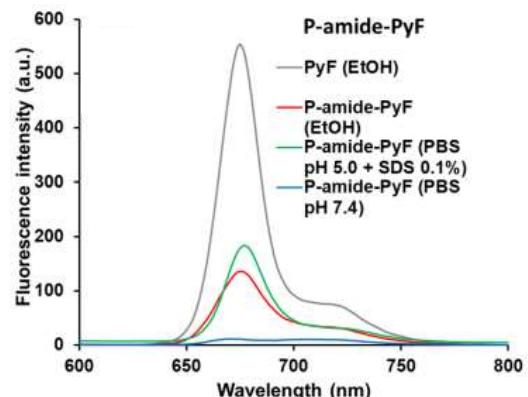
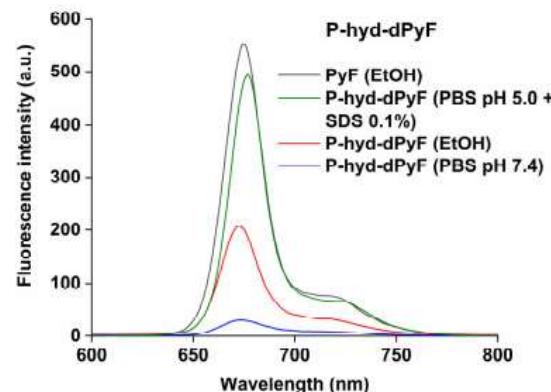
Aim of the study



Synthesis

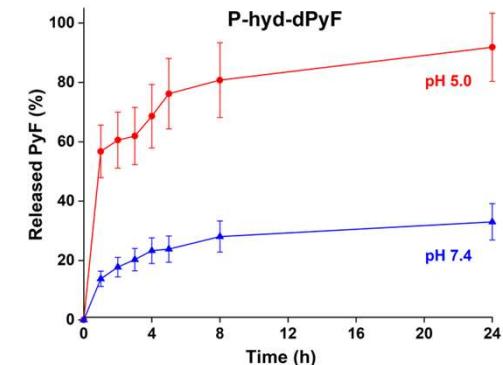


Quenching and activation of fluorescence

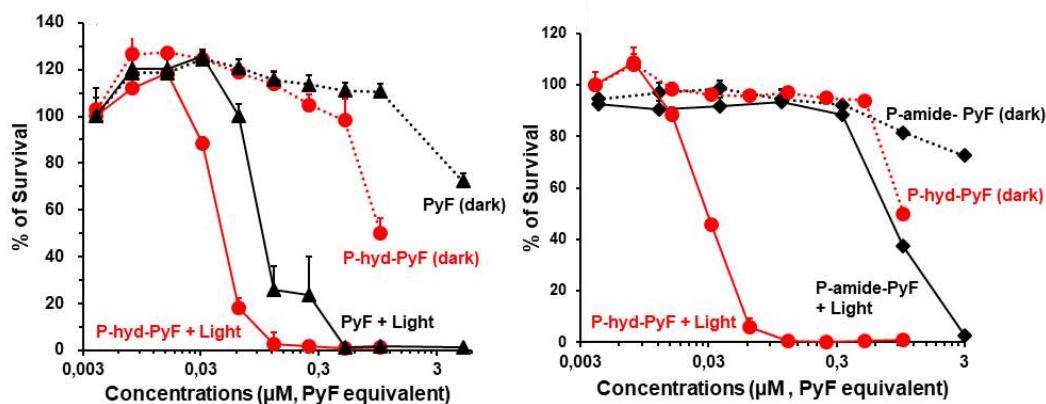


- The activation in acidic conditions was observed
- The fluorescence and ${}^1\text{O}_2$ generation is depleted after formation of micelles
- Full restoration of activity after disruption of the micelles and release of PyF

pH-sensitive behavior

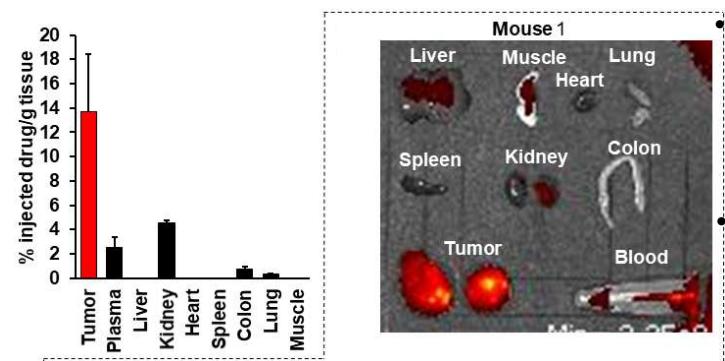


Dark and light cytotoxicity



- The P-hyd-dPyF conjugate showed similar dark toxicity as free PyF or nondegradable P-amide-PyF
- After illumination with light the P-hyd-dPyF showed much stronger cytotoxicity when compared to the P-amide-PyF or free PyF

Biodistribution

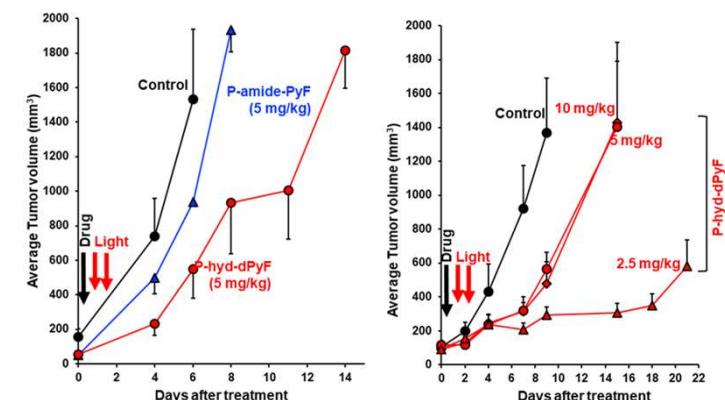


The fluorescence signal was observed predominantly from the tumorous tissue, with excellent ration to liver. Almost all major organs were free of the fluorescent activity of the nanotheranostics.

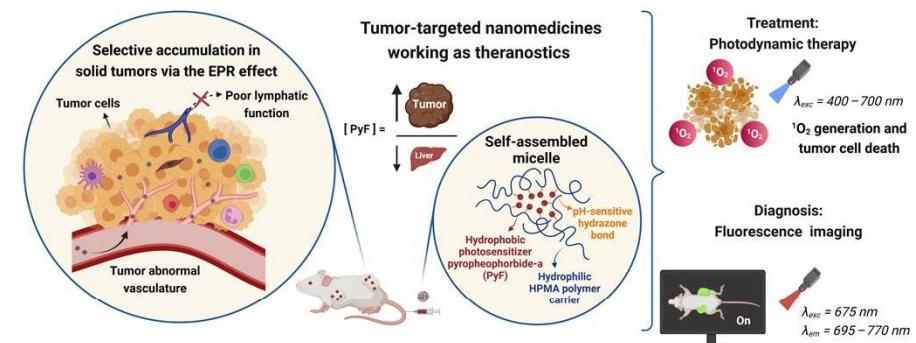
Conclusion

- The pH-sensitive theranostics was developed by employing the dPyF derivative and biocompatible copolymer*
- The theranostics is completely switched off during the delivery and activated in the tumorous tissue*
- The predominant tumor tissue accumulation was found showing the excellent diagnostics potential of the system*
- The excellent efficacy was found for low dose treatment using the developed theranostics*

In vivo therapeutic efficacy



- The P-Hyd-dPyF showed higher efficacy than nondegradable polymer system and free PyF
- Reversed dose dependence was found showing the excellent activity in low dose treatment of tumors



Tavares M, Etrych T., Theranostics 13 (2023) 4952

Acknowledgement.



Financial support:



Co-funded by
the European Union



Thank you for your attention

