Site-selective Protein Modification Chemistry for Basic Biology and Therapeutics

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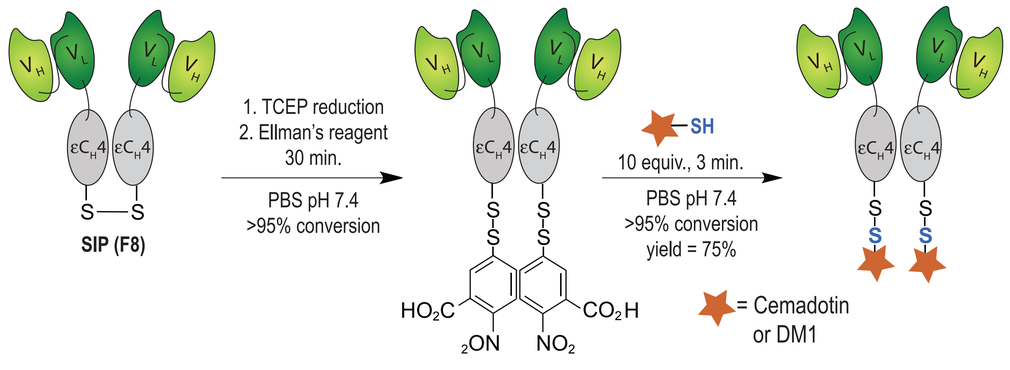
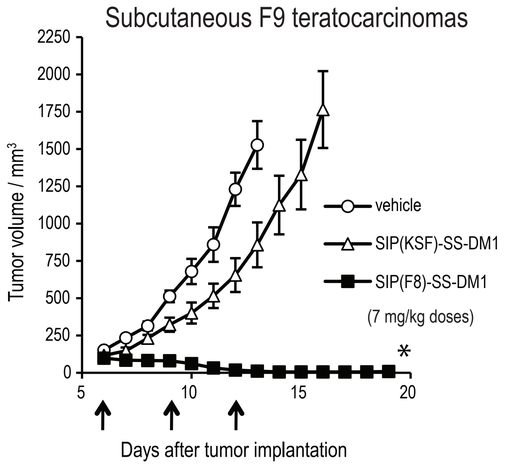
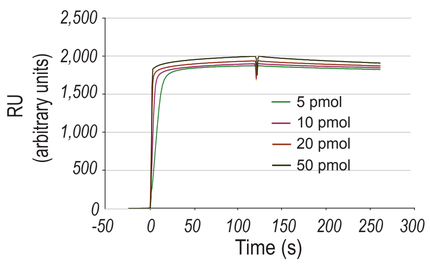
Traceless Vascular Targeting Antibody-drug Conjugates (ADCs)

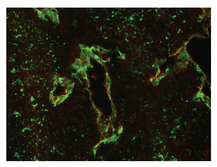
Targeted delivery of potent drugs to the tumor neovasculature as a novel strategy for cancer therapy. The resulting traceless, chemically-defined ADC potently inhibits tumor growth in different syngeneic immunocompetent models of murine cancer.



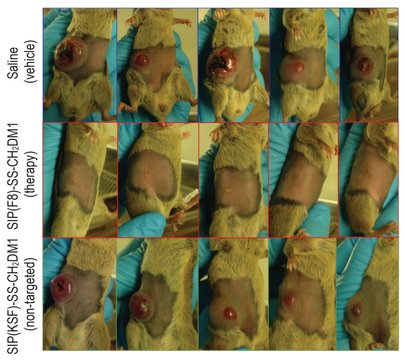
Bernardes GJL; Steiner M; Hartmann I; Neri D & Casi G *Nature Protocols* **2013**, *8*, 2079

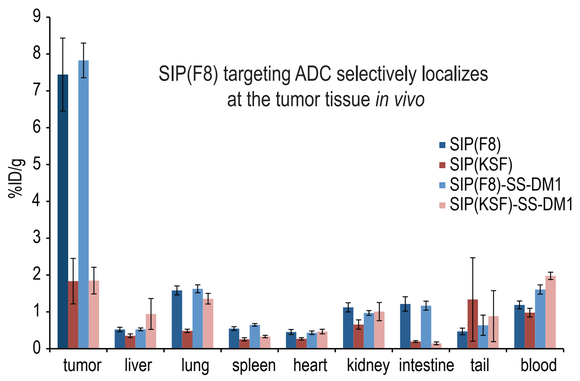




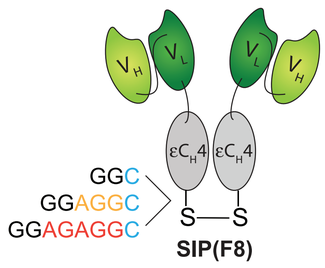


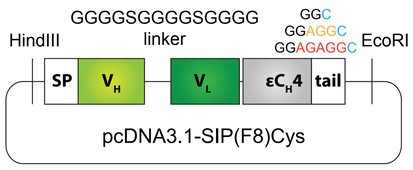
SIP(F8) targeting ADC remains immunoreactive & selectively localizes and recognizes neo-vasculature structures



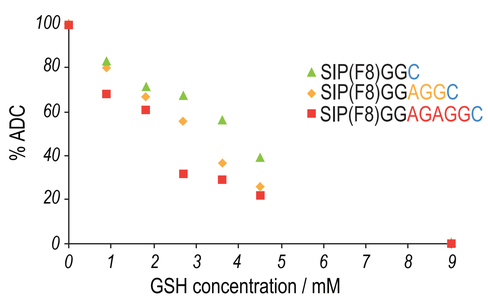


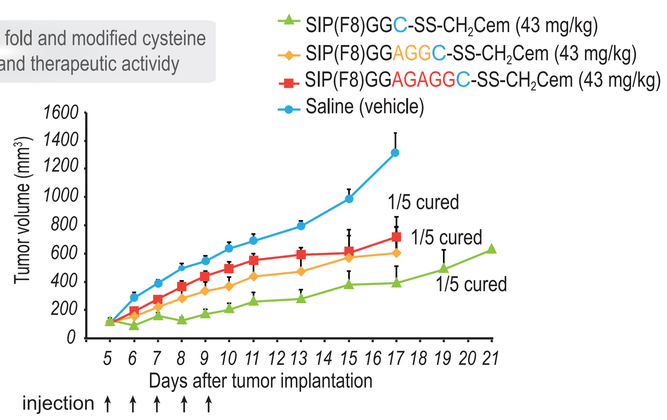
Bernardes GJL; Casi G; Trüssel S; Hartmann I; Schwager K; Scheuermann J & Neri D
Angew. Chem. Int. Ed. **2012**, *51*, 941. VIP Paper.
Perrino E; Steiner M; Krall N; **Bernardes GJL**; Pretto F; Casi G; Neri D
Cancer Res. **2014**, doi:10.1158/0008-5472.CAN-13-2990.





distance between antibody fold and modified cysteine influence drug release and therapeutic actividy





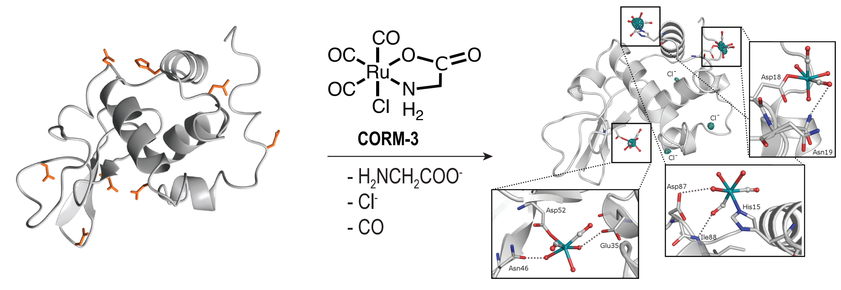
Steiner M; Hartmann I; Perrino E; Casi G; Brighton S; Jelesarov I; **Bernardes GJL***; Neri D *Chemical Science*, **2013**, *4*, 297.

Controlled Delivery of Therapeutic CO for the Treatment of Cancer

As a result of its signalling functions, carbon monoxide (CO) is involved in a multitude of defence mechanisms in physiologic and pathologic situations. My group is currently exploring (i) the use of synthetic carbonyl metalloproteins for the saptiotemporal controlled delivery of CO *in vivo* and (ii) CO's immunomodulatory properties for the treatment of cancer

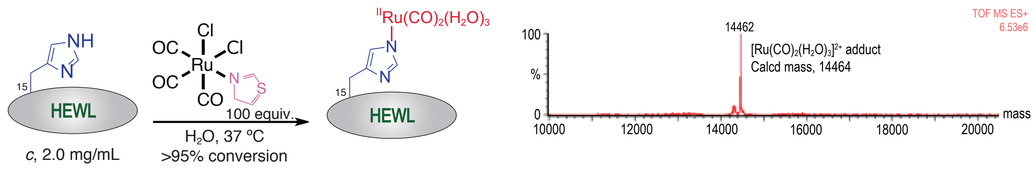
Seixas JD; Blättler WA; Romão CC & **Bernardes GJL*** *Chem. Soc. Rev.* **2012**, *41*, 3571.
García-Gallego S & **Bernardes GJL*** *Angew. Chem. Int. Ed.* **2014**, *53*, 9712.

Interactions of CORM-3 with transport proteins studied by X-ray

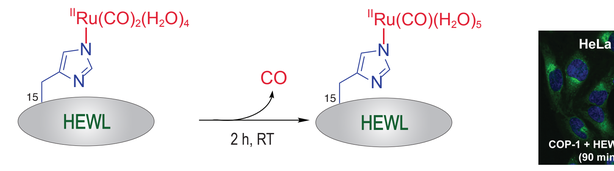


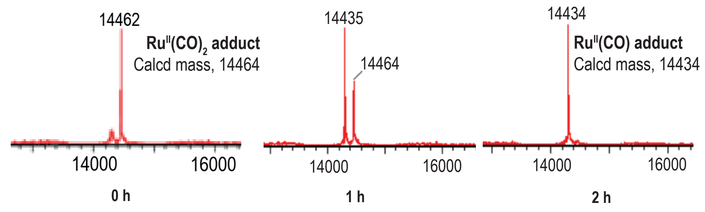
Santos-Silva T; Mukhopadhyay A; Seixas JD; **Bernardes GJL*;** Romão CC; Romão MJ
J. Am. Chem. Soc. **2011**, *133*, 1192.

Ruthenium carbonyl metalloproteins as CO carriers



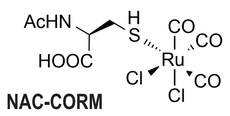
controlled CO release from chemically-defined metalloproteins



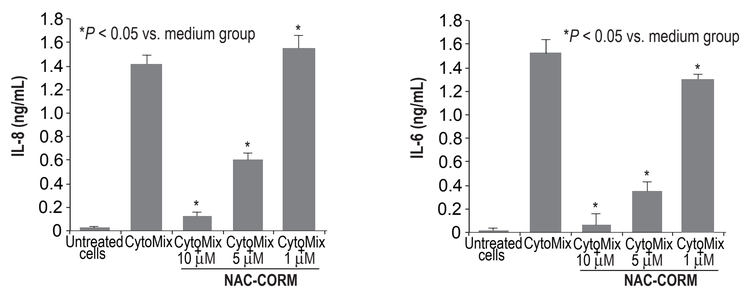


Chaves-Ferreira M & **Bernardes GJL*** *manuscript submitted.*

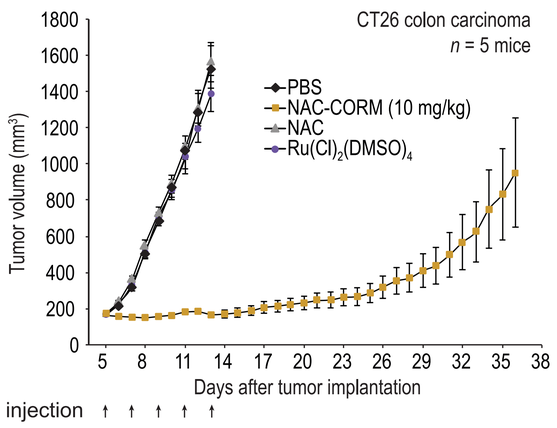
Exploring CO immunomodulatory effect for cancer therapy

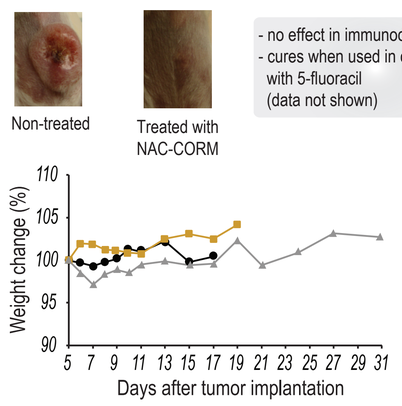


- aqueous soluble
- residual CO-Hb levels
- does not induce ROS
- non-cytotoxic



Downregulation of pro-inflammatory cytokines, TNF-α and IL-6, and angiogenic chemokine, IL-8, leads to a strong tumour growth inhibition in an immunocompetent mouse model of cancer





- no effect in immunodeficient mice
- cures when used in combination with 5-fluoracil (data not shown)

Chaves-Ferreira M & **Bernardes GJL*** *manuscript under preparation*

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