

Dipartimento di Biotecnologie e Bioscienze – UNIMIB

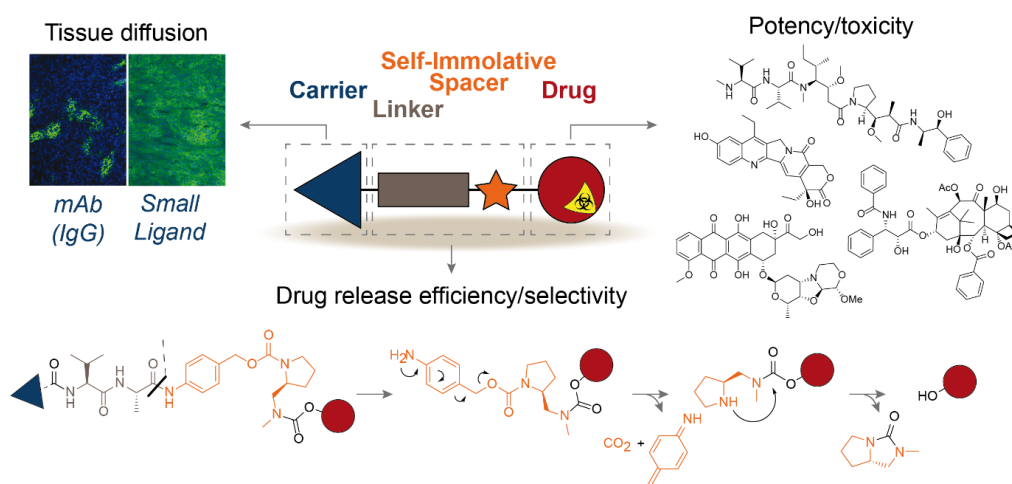
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# “Chemical Design of Tumor-Targeted Drug Conjugates”

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**Abstract:** The covalent conjugation of potent cytotoxic agents to either macromolecular carriers (e.g. monoclonal antibodies) or small molecules (i.e. peptides and small ligands) represents a well-known approach to increase the therapeutic index of these drugs, thus improving treatment efficacy and minimizing side effects. While the carrier is fundamental to modulate the drug biodistribution *in vivo*, the cytotoxic activity is displayed only upon cleavage of a specific chemical bond (linker) that connects the drug to the carrier. The perfect balance between the linker stability and its selective cleavage represents the key for success in these therapeutic approaches. Moreover, different types of “self-immolative” spacers are often installed between linker and drug fragments, either acting as chemical adaptors or to facilitate the prodrug activation.<sup>[1]</sup> New strategies to improve the efficacy of Tumor-Targeted Drug Conjugates will be discussed here, ranging from the design of non-internalizing conjugates,<sup>[2]</sup> to novel self-immolative spacers for drug activation.<sup>[3]</sup>



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