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Erratum

Arresting Cancer Proliferation by Small-Molecule Gene Regulation

Liliane A. Dickinson,[1] Ryan Burnett,[1] Christian Melander,[1] Benjamin S. Edelson,[2] Paramjit S. Arora,[2] Peter B. Dervan,[2,*] and Joel M. Gottesfeld[1,*]
[1] Department of Molecular Biology
The Scripps Research Institute
La Jolla, California 92037
[2] Division of Chemistry and Chemical Engineering
California Institute of Technology
Pasadena, California 91125

*Correspondence: dervan@its.caltech.edu (P.B.D.); joelg@scripps.edu (J.M.G.)

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In this paper by Dickinson et al., the structures of the polyamide-chlorambucil (Chl) conjugates shown in Figure 1 are incorrect.

These molecules are α linked, not γ linked hairpins, as shown. This was the result of the use at Scripps of Boc-D-Dab (Fmoc)-OH rather than Fmoc-D-Dab(Boc)-OH, which afford constitutional hairpin isomers. The correct structure of 1R-Chl is shown below. All other polyamides used by Dickinson et al. had the same α linkage. α- and γ-linked hairpins have similar DNA binding properties. The polyamide-Chl conjugates display different DNA alkylation reactivity, in which the γ polyamides are more reactive than α. In fact, the synthetic error was discovered when the Caltech team synthesized for scale up the γ-linked molecules, and they were found to be significantly more toxic in mice than the corresponding α-linked molecules. The serendipitous finding that hairpin polyamides with different turn units have very different toxicities would not have been anticipated. Importantly, the key data in the paper have been reproduced at Scripps and Caltech, and the conclusions of the paper are unchanged. We will report in due course a detailed comparison of the two classes of molecules.

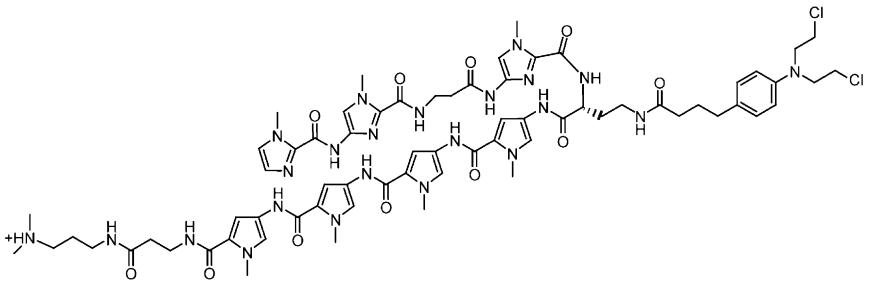

Figure 1. Polyamide Conjugate Structure

1R-Chl = ImIm-β-Im-α(*R*-2,4-DABA^{Chl})-PyPyPyPy-β-Dp, in which Py is pyrrole, Im is imidazole, β is β-alanine, Dp is dimethylaminopropylamine, and 2,4-DABA is (*R*)-2,4-diaminobutyric acid with α describing the amino acid linking the polyamide and Chl describing the chlorambucil substituent at the 4-amino position.

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