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Venue:	Biochimie, Vol. 160, May 2019
Title:	Article: The C-7 aminomethylpyrrolidine group rescues the activity of a thiofluoroquinolone
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Туре:	Article
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Abstract (or Book Review):	A Mg ²⁺ -water bridge between the <i>C</i> -3, <i>C</i> -4 diketo moiety of <u>fluoroquinolones</u> and the conserved <u>amino acid</u> residues in the GyrA/ParC subunit is critical for the binding of a fluoroquinolone to a topoisomerase-DNA covalent complex. The fluoroquinolone UING-5-249 (249) can bind to the GyrB subunit through its C7-aminomethylpyrrolidine group. This interaction is responsible for enhanced activities of 249 against the wild type and quinolone-resistant mutant topoisomerases. To further evaluate the effects of the 249-GyrB interaction on fluoroquinolone activity, we examined the activities of decarboxy- and thio-249 against <u>DNA gyrase</u> and conducted docking studies using the structure of a gyrase-ciprofloxacin-DNA <u>ternary complex</u> . We found that the 249-GyrB interaction rescued the activity of thio-249 but not that of decarboxy-249. A C7-group that binds more strongly to the GyrB subunit may allow for modifications at the <i>C</i> -4 position, leading to a novel compound that is active against the wild type and quinolone-resistant pathogens.