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Discovery of Novel Fluoroquinolone Antibiotics WFQ-101 and Its Optimization Study

○ Tatsuya HIRANO[1], Tomohiko KINOSHITA[1], Daichi KAZAMORI[1], Satoshi INOUE[1], Kouji NISHIMURA[1], Asuka SAKURAI[1], Ayuka SASAKI[1], Yasuhiro KURAMOTO[1], Hirotaka AMANO[1], Akira YAZAKI[1]

[1]Drug Discovery Laboratory, Wakunaga Pharmaceutical Co., Ltd.

As the difficult-to-treat infections caused by multidrug-resistant bacteria have spread, it is an urgent need to develop novel antibiotics for the treatment of them. Therefore, we started the research to discover novel antibiotics with potent antibacterial activities, especially against Gram-negative resistant pathogens.

Recently, we evaluated the minimum inhibitory concentration (MIC) of our quinolone library for *P. aeruginosa* with or without the efflux pump inhibitor PAβN. We found that the MICs of a certain type of compounds such as WFQ-101, having 2-hydroxymethylphenyl group at 1-position, were less changed by the presence of PAβN, indicating the possibility to overcome the drug resistance by bacterial efflux system. We selected WFQ-101 as a lead compound and have continued its structural optimization. For example, an introduction of 5-methyl group drastically increased the activity, whereas the modification of 7-substituent, such as the increases of lipophilicity and/or bulkiness, was not tolerated for the activity against Gram-negative pathogens. In this presentation, we will describe the results of our optimization study, demonstrating the Structure-Activity Relationship.