

## Summary of VBL Research Project

<b>Theme</b>	Automatic Synthesis of Pyrrole-imidazole Polyamide by Flow-reaction
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Pyrrole-imidazole polyamide (PIP) is a peptide composed of pyrrole (Py) and imidazole (Im), which can specifically recognize and bind the base sequence of DNA. Therefore, molecular creation that directly acts on targeted DNA by binding a pharmacologically active unit to PIP has been studied. However, the mainstream of chemical synthesis of PIP is the method using a polymer called solid-phase synthesis method, which requires a large number of reagents and can only synthesize in a few mg scales and also discharges polymer waste. Therefore, we planned to develop a new methodology for the synthesis of PIP inexpensively and in large quantities and decided to use flow chemistry for the fully automatic synthesis. The flow method has advantages compared with the batch method through a perspective of manufacturing: easy to scale up, shorten the reaction time, and control the reaction temperature. It is also an advantageous feature of flow method that the reaction can be performed in series by connecting the flows. Thus, using the flow method, we thought that it was possible to synthesize any sequence and length of PIP by just pressing a button of pumps. Under these plans, we started the flow synthesis of PIP, and until now we have succeeded in efficiently synthesizing up to any dimer to tetramer of PIP by combining the batch method and the flow method (patent application: 2019-049328). However, this preparation method of PIP requires the purification after each reaction. Hence, in this VBL research, we challenge the fully automatic synthesis of PIP by sequential flow method.

