Synthesis of ADC Linker payload

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SN38: a novel payload for ADC development

SN38 is an antineoplastic drug. It is the active metabolite of irinotecan (an analog of camptothecin—a topoisomerase I inhibitor) but is 1000 times more active than irinotecan. So far, two ADCs bearing SN38 as payload, both developed by Immunomedics, have entered clinical trials. CIBL has extensive experience with SN38-related payload-linker synthesis. The successful cases include the synthesis of Mc-vc-PAB-SN38, a relatively simple synthesis involving 3 steps, and that of CL2A-SN38 (proprietary for Immunomedics), a much more complex construct that requires 10-step synthesis.

Case 1: Mc-vc-PAB-SN38

Synthesis route design:
Based on the structure of Mc-vc-PAB-SN38, a 3-step synthesis route was designed.

Case 2: CL2A-SN38

Synthesis route design:
Based on the structure of CL2A-SN38, a 10-step synthesis route was designed.

Results
Mc-vc-PAB-SN38 was successfully synthesized in 3 weeks. Final product is characterized as:
1. Purity > 95% by LC-MS

Results
CL2A-SN38 was successfully synthesized in 10 weeks. Final product is characterized as:
1. Purity validated by 1HNMR
2. Structure confirmation: compound structure validated by 1HNMR

Conclusions
1. Using the “DrugLink” custom synthesis service, Creative Biolabs successfully synthesized two SN38-linker complexes.
2. “DrugLink” custom synthesis service is well-suited for simple synthesis tasks with only a few steps and complex organic synthesis with multiple steps (in this case, a 10-step synthesis was successfully demonstrated).
3. The compounds prepared by the “DrugLink” custom synthesis service are correct in structure and show excellent purity.

References

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