

SUMMARY-OF-INVENTION

[0004] This disclosure provides a method to produce a full-length antibody comprising a heavy chain (HC) and a light chain (LC) in high yield. The method comprises culturing *E. coli* cells expressing a coding sequence for the HC and a coding sequence for the LC under conditions permissible for producing the HC and LC, and the full-length antibody can be produced in an amount of at least 200 mg/L. In some embodiments, the full-length antibody is produced at a wet weight percentage in a range from 0.05% to 20%, from 0.05% to 10%, from 0.05% to 5%, or from 0.05% to 1% relative to the weight of wet cell pellet produced from the *E. coli* cells in the culture. In some embodiments, at least some of the *E. coli* cells contain an oxidative cytoplasm. In some embodiments, the method comprises transforming the plasmid to the *E. coli* strain. In some embodiments, the HC and LC are produced in the cytoplasm of the *E. coli*. In some embodiments, the method further comprises assembling the produced HC and LC under non-reducing conditions to form the full-length antibody. In some embodiments, the molar ratio of the produced HC and the produced LC from the *E. coli* is 1:1 to 1:3.

[0004a] In an aspect, disclosed herein is a method to produce a full-length antibody comprising a heavy chain (HC) and a light chain (LC), wherein the method comprises: culturing *E. coli* cells expressing a coding sequence for the HC and a coding sequence for the LC under conditions permissible for producing the HC and LC in a culture medium, and wherein the full-length antibody is produced in an amount of at least about 200 mg per liter of the culture medium, or wherein the weight percentage of the full-length antibody produced relative to the weight of cell pellet produced from the *E. coli* cells is in a range from 0.05% to 20%.

[0005] In some embodiments, expression of HC, LC, or both is controlled by a promoter, for example, a T7 promoter or a promoter that has substantially similar promoter strength as the T7 promoter. In some embodiments, the plasmid comprises a bicistronic operon, wherein the bicistronic operon comprises the coding sequence for the HC and the coding sequence for the LC. The bicistronic operon may comprise a promoter that drives expression of both the HC and LC, and the promoter is a T7 promoter or a promoter that has substantially similar promoter strength as the T7 promoter. In some embodiments, the bicistronic operon comprises a T7 terminator. In some embodiments, the plasmid encoding the HC and LC comprises a first monocistronic operon for the HC and a second monocistronic operon for LC. In some embodiments, the first operon comprises a

ribosomal binding site that comprises a sequence selected from any of SEQ ID NO: 18-20 and the second monocistronic operon comprises a ribosomal binding site comprising the sequence of SEQ ID NO: 17. In some embodiments, the first monocistronic operon or the second monocistronic operon each independently comprise a T7 promoter or a promoter that has substantially similar promoter strength as the T7 promoter. In some embodiments, the first or second monocistronic operon each independently comprise a T5 promoter, or a promoter that has substantially similar promoter strength as the T5 promoter. In