Researchers reveal a unique, hitherto-unknown bacterial transcriptional promoter recognition mode

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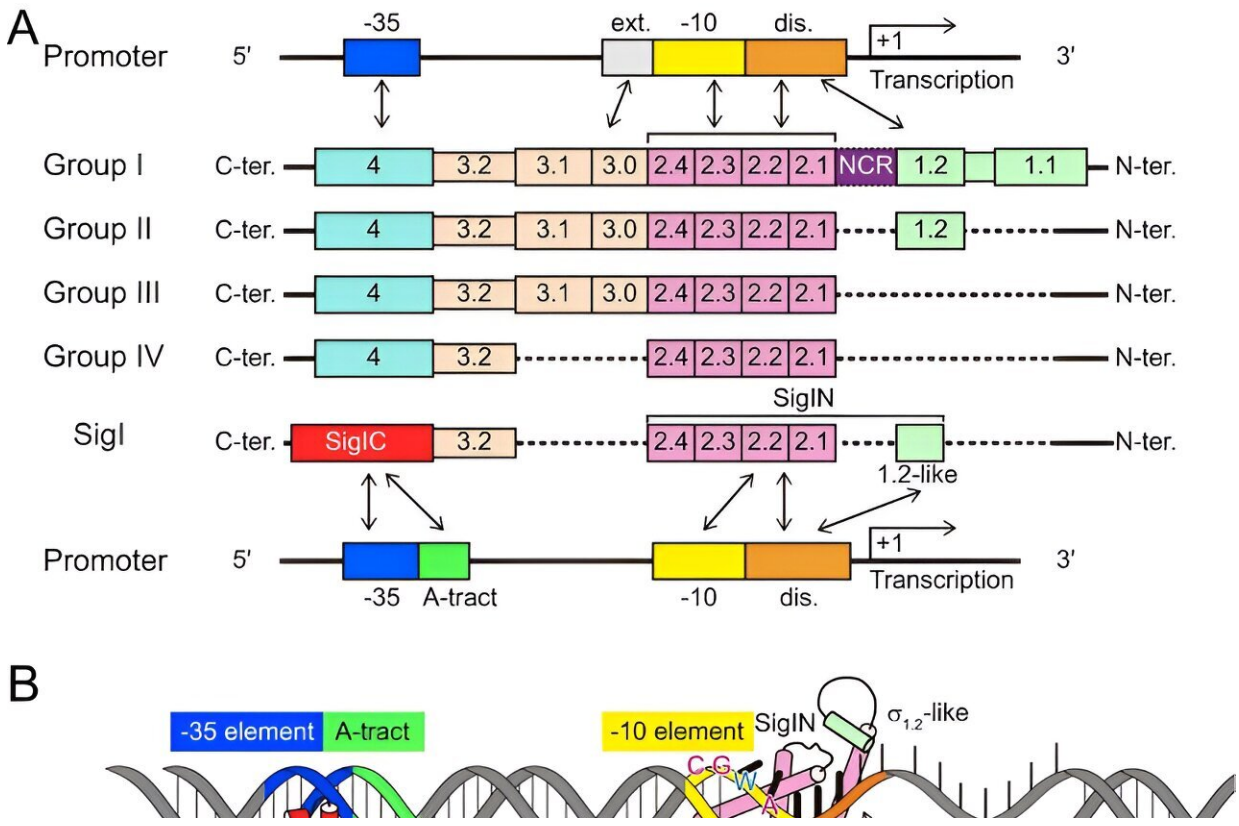

Schematic diagrams of the promoter recognition by σ^{I} and by the four groups of σ^{70} family σ factors. Credit: Feng Yingang & Zhu Ping's group

Researchers led by Prof. Zhu Ping from the Institute of Biophysics and

Prof. Feng Yingang at the Qingdao Institute of Bioenergy and Bioprocess Technology, both under the Chinese Academy of Sciences, have revealed a unique, hitherto-unknown bacterial transcriptional promoter recognition mode by distinct σ^I factors in Clostridium thermocellum, both with respect to domain organization and binding mode to promoter DNA.

The study was published in *Nature Communications* on Oct. 13.

Lignocellulose can be efficiently degraded by a class of anaerobic clostridia represented by C.thermocellum through a secreted multienzyme complex, termed cellulosome, which is of great value in the development of bioenergy.

Bacterial σ factors are critical components of RNA polymerase (RNAP) holoenzymes for initiation of transcription by specifically recognizing DNA promoter regions. A single bacterium often contains multiple σ factors. However, the σ^I (SigI) in C. thermocellum exhibits lower homology to most σ factors and stands as a unique member within the bacterial σ factor family σ^{70}.

To reveal the molecular mechanism of how the SigI factors in C. thermocellum recognize promoters, the researchers prepared a ternary complex formed by SigI, RNAP, and promoter DNA, and determined the cryo-EM structures of RNAP-σ-promoter open complexes (RPo complexes) of two C. thermocellum σ^I complexes, i.e., RPo-SigI1 and RPo-SigI6 complexes, in the active state at 3.0Å and 3.3Å resolution, respectively.

Comparing the structures of these two RPo-SigI complexes with those of other transcriptional complexes, the researchers found that although the SigI-mediated transcriptional open complex presented an overall conserved architecture, SigI exhibited a distinctive promoter recognition

mechanism among other σ factors in σ^{70} family.

The C terminal domain of SigI (SigIC) presented a unique -35 element recognition mode. SigIC bound the DNA major groove of promoter -35 element through its helix-turn-helix (HTH) motif, which was rotated about 180° compared to the HTH binding in the major groove of σ_4 domain of other σ factors in the σ^{70} family. In addition to the binding with the major groove, SigIC also inserted a conserved histidine into the DNA minor groove of -35 element, which is the conserved A-tract region of the promoter, representing a unique promoter recognition mode of SigI factors.

The recognition mode to the promoter -10 element by the N terminal domain of SigI (SigIN) also showed novel features: the SigIN domain had a conserved interaction mode with CGWA motif of -10 element while all transcription-bubble bases in -10 element interacting with SigIN were flipped out, which formed extensive protein-nucleic acid interactions with SigIN. These interactions may modulate the promoter activity and determine the differences in the transcription strength of SigI-dependent promoters of cellulosomal genes.

The study indicates that the transcriptional regulatory factor σ^I in C. thermocellum possesses a unique promoter recognition mechanism. This finding holds implications for understanding how C. thermocellum regulates the expression of cellulase genes and for the modification and application of its cellulases.

Additionally, the distinctiveness of σ^I factor in its promoter recognition mechanism enriches our understanding of the diversity of microbial transcriptional regulation.

More information: Jie Li et al, Structure of the transcription open complex of distinct σ^I factors, *Nature Communications* (2023). DOI:

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