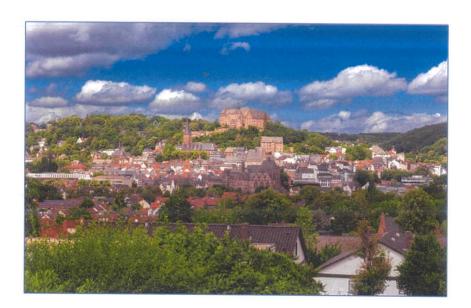
6th European NF-kappaB Workshop

Monday 02 September 2024 - Wednesday 04 September 2024 Vila Vita Rosenpark, Marburg



Book of Abstracts



Venue



Vila Vita Rosenpark
Hotel & Residenz Rosenpark
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All sessions will take place in the
"Vivaldi" room (basement floor of
hotel)

Organisers



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The regulation of transcriptional activation by NF-κB p52 homodimer and proto-oncogenic Bcl3

Author: Vivien Ya-Fan Wang¹

The binding of transcription factors (TFs) to their specific DNA response elements in the promoters/enhancers of target genes is the key event regulating gene transcription and consequent cellular events. The NF-kB family of TFs plays a critical role in diverse physiological processes. Our study focuses on the transcriptional regulation by one NF-κB family member, p52, and its specific cofactor, B-cell lymphoma 3 (Bcl3). Bcl3 is an oncoprotein, the constitutive nuclear presence of Bcl3 induces chronic inflammation and proliferation. Bcl3 is also extensively phosphorylated, it associates with NF-kB p52 homodimers to regulate transcription. Using the combination of structural and biochemical studies, we have shown 1) Bcl3 plays an essential role in enhancing p52:p52 homodimer population in cells which is an unique mechanism to p52 within NF-kB family. 2) Crystal structures of p52:p52 homodimer in complex with its natural kB DNA target site(s) revealed a widening of the DNA minor groove compared to all previously known structures of NF-κB-DNA complexes; further MD simulations studies provide new insights into allosteric control by closely related κB DNAs on NF-κB-dependent transcriptional specificity. 3) Phospho-modification mediated changes in Bcl3 regulate DNA accommodation by the Bcl3:(p52:p52) complex. Overall, our studies shed lights on the intricate structural changes driven by both DNA and protein conformation and dynamic states in modulating transcriptional activity.

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