

Supplementary Information 3 | **ATF/CREB Interactions with JUN
& Tumorigenic Implications**

<u>ATF/CREB Family Member</u>	<u>Known Interaction with Jun</u>	<u>Implication in tumorigenic transformation</u>
ATF-1	Probable interactions with JUN in intestinal inflammation model ¹ .	Involvement in hypoxic response ² and in inflammatory response ³
ATF-2	JUN binding in cancer ^{4,5} .	Multiple ATF2 transcriptional alterations in cancer ^{4,6} .
ATF-3	JUN binding during E1A-mediated transformation ⁷ . ATF3 dimerization with JUN mediates Ras signaling, while dimerization with JunD abrogates signaling ⁸ .	Highly probably Jun binding during cellular transformation and neuronal survival response ^{8,9} . ATF3 promotes growth factor independence in chicken embryonic fibroblasts ¹⁰ .
ATF-4 (CREB2)	Suggested competitive binding of Jun between ATF-2 and ATF-4 to modulate cyclin A signaling ¹¹ .	Loss of ATF4 abrogates H-Ras transformation ¹² . Increased ATF2 expression in leukemia ¹³ . Loss of ATF4 promotes loss of osteoblast differentiation ¹⁴ .
ATF-5 (ATFx)	N/A	Increased ATF5 expression in Hodgkin's lymphoma ¹⁵ .
ATF6a	N/A	Increased expression in hepatocarcinoma ¹⁶ . ATF6a required for tumor cell survival via Rheb-mTor pathway ¹⁷ .
ATF-7 (ATFa)	Binding with Jun and Fos via TAF4, which modulate transcriptional activity ^{18,19} .	Upregulation of ATF7 in human cervical cancer ²⁰ . Implicated in anti-apoptotic

		signaling ²¹ .
B-ATF	Demonstrated binding to JunB, JUN, JunD, and to a lesser extent, to c-Fos ²² .	B-ATF functions as tumor suppressor ²³ .
CREB	Demonstrated binding with JUN ^{24,25} .	CREB plays multiple roles in tumorigenesis ^{26,27} .
CREM	Demonstrated not to bind to Jun, but to antagonize Jun transcription via competitive promoter binding ²⁸ .	Increased CREM expression in adrenocortical and lung carcinoma ^{29,30} . Upregulation by HTLV-1 ³¹ .
JDP-1	Demonstrated to bind JUN, but to a much lesser extent than JDP-2 ³² .	Expression correlates with estrogen receptor status in breast cancer ³³ .
JDP-2	Demonstrated to bind JUN ^{32, 34} .	JDP2 functions as tumor suppressor ³⁵ .

Legend

Known interactions between ATF family members and JUN and tumorigenic implications.

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