

4. JNK induces two genes encoding the **Fos and Jun TFs**. Once they are synthesized, these two proteins, c-jun and c-fos, they can associate with one another to form **AP-1**, a widely acting heterodimeric TF that is often found in hyperactivated form in cancer cells.
5. Gene transcription and cell growth downstream of the AP-1 complex has a positive feedback mechanism, which leads to increase transcription of c-jun and c-fos.
6. **p38**, on the other hand, phosphorylates **ATF-2** (attached to c-jun) and **MEF-2**, which lead to the activation of c-fos, thus **promoting cell proliferation and survival**.
7. Melanoma's have strong nuclear ATF-2 expression that correlates with metastasis. Pancreatic cancer has somatic mutations of *Jnk* and *Atf2* in pancreatic cancer cell lines.
8. As you can see, several retroviral oncogenes are derived from genes for nuclear transcription factors, such as *fos*, *jun*, *myc* etc.

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