

***Xenopus* FANCG contains highly conserved domains and is subject to alternative splicing during the earliest stages of vertebrate development**

Stacie Stone, Margriet van Kogelenberg, Alexandra Sobeck, Bendert de Graaf, Maureen Hoatlin

Division of Molecular Medicine, Oregon Health & Science University, Portland, Oregon

We recently identified the *Xenopus laevis* homolog of FANCG (xFANCG) for our ongoing biochemical studies of the FA protein pathway in *Xenopus* cell-free egg extracts. The predicted protein sequence of xFANCG is 46% similar and 34% identical to human FANCG. Comparison between human and xFANCG suggests that three of the seven TPR (tetratricopeptide repeat) domains, as well as the N-terminal leucine zipper are highly conserved. The FANCG TPR protein-protein binding motifs are thought to participate in interactions among FA proteins including FANCA. Although the overall homology of the human and *Xenopus* FANCG proteins is relatively low, the conservation of the leucine zipper and TPR motifs 1,2, and 4 is striking.

Expression of *xFANCG* was evaluated by RT-PCR during *Xenopus* development. We found that *xFANCG* is expressed throughout development, and alternatively spliced variants were present after the midblastula transition when zygotic transcription/translation begins. One splice variant is predicted to encode a FANCG protein that skips exon two, and uses an alternative start codon within exon one. Exon skipping is thought to represent functionally regulated alternative splicing as opposed to aberrant splicing. These observations are important because they suggest FANCG protein variants could be regulated during vertebrate development, possibly to modulate FANCG binding to previously described protein partners such as FANCA, FANCF, and/or BRCA 2.

(Stacie Stone)