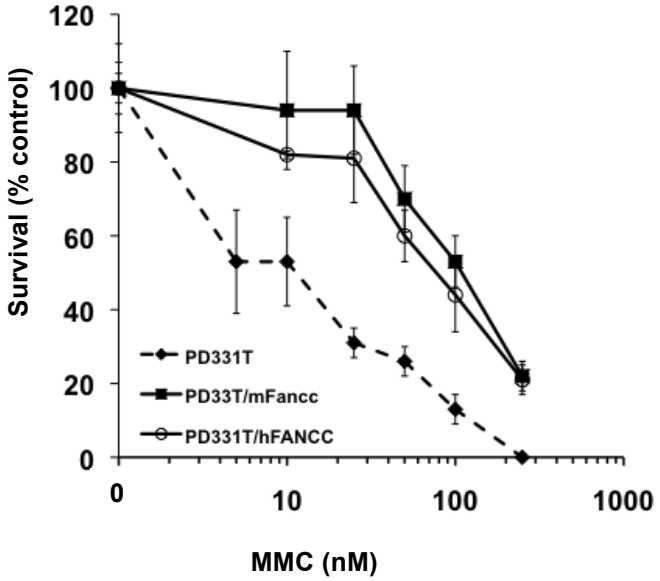

Figure S1. *mFancc* and *hFANCC* correct the MMC hypersensitivity of hFANCC-deficient human fibroblasts. Survivals of transformed hFANCC-deficient human fibroblasts (PD331T) transduced with *hFANCC* (PD331T/*hFANCC*) or *mFancc* (PD331T/*mFancc*) and treated with MMC for 5 days (means ± S.D. from one of two similar experiments performed in triplicate.) PD331T cells ($EC_{50} \cong 10$nM) were approximately ten-fold more sensitive to MMC than PD331T/*hFANCC* or PD331T/*mFancc* ($EC_{50s} \cong 100$nM).

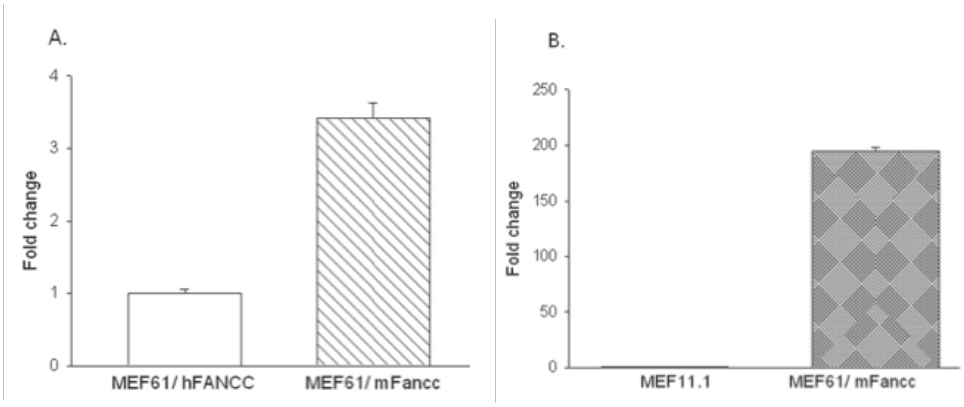

Figure S2. Comparative mRNA levels of *mFancc* and *hFANCC* in MEFs *A*. The mRNA levels of transduced *hFANCC* and *mFancc* were measured in Fancc-deficient MEFs (MEF61) by Real-time PCR and expressed as 18S rRNA-normalized relative-fold change over *hFANCC* levels. Primers were designed to hybridize with viral (pLXSH) sequences expressed in both *hFANCC/mFancc* RNA transcripts. Values represent means ± S.D. from one similar experiment of two performed in triplicate. *mFancc* expression was approximately three-fold higher than *hFANCC*. *B*. *mFancc* RNA levels (probes were desgined to hybridize with *mFancc* coding sequence) were measured by Real-time PCR in wild-type MEFs (MEF11.1) and Fancc-deficient MEFs transduced with *mFancc* (*MEF61/mFancc*). Levels are expressed as relative-fold change over MEF11.1 levels and values represent means ± S.D. from one experiment performed in triplicate. Transduced levels of *mFancc* were approximately 200-fold higher than endogenous levels in wild-type MEFs. Extrapolating results from above (*A*), the level of *hFANCC* expressed in MEF61 cells is then roughly 67-fold higher than endogenous levels of *mFancc* in wild-type cells.

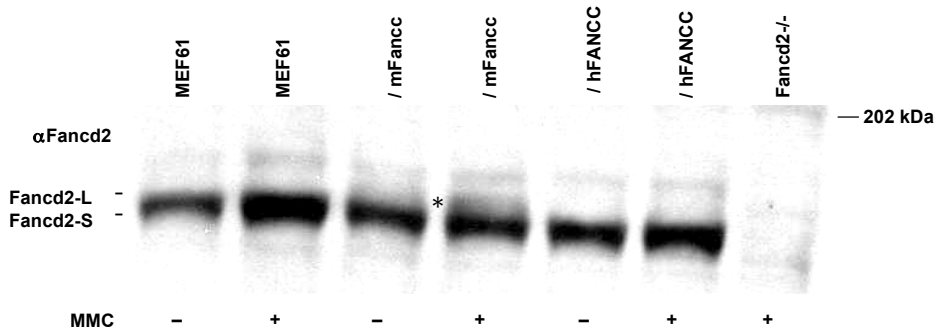

Figure S3. mFancc, but not hFANCC facilitates mFancd2 ubiquitination. Immunoblot of whole cell lysates from MEF61 cells (Fancc-deficient) transduced with *hFANCC* or *mFancc*. *Fancd2*$^{-/-}$ cells were isolated from Fancd2-deficient mice. Cells were treated ± MMC for 24 hours and incubated with anti-Fancd2 antibody (Abcam; 1:2000). *= mono-ubiquitinated Fancd2 (Fancd2-L).

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Human 1      MAQDSVDLSCDYQFWMQKLSVWDQASTLETQQDTCLHVAQFQEFLRKMYEALKEMDSNTV 60
             MAQ+S DL+ D Q W+QKLS W+QAS+ ETQ+DTCLH++ FQEFLR+MYE LKEMDS+ +
Mouse  1     MAQESADLASDCQSWLQKLSAWEQASSEETQKDTCLHLSGFQEFLRQMYEILKEMDSDAI  60

Human  61    IERFPTIGQLLAKACWNPFILAYDESQKILIWCLCCLINKEPQNSGQSKLNSWIQGVLSH  120
             +ERFPTIGQLLAKACWNP ILAYDESQKI+IWCLCCL+NKEP+ S +S LNSWI+G+LSH
Mouse  61    LERFPTIGQLLAKACWNPLILAYDESQKIVIWCLCCLMNKEPRTSAESGLNSWIRGLLSH  120

Human  121   ILSALRFD-KEVALFTQGLGYAPIDYYPGLLKNMVLSLASELRENHLNGFNTQRRMAPER  179
             +LSA RFD KEV LFT+ LGY  IDYYP LLKNMVLSL SELRE+HLNG +TQ RMAPER
Mouse  121   VLSAFRFDMKEVCLFTKSLGYESIDYYPSLLKNMVLSLVSELRESHLNGLSTQSRMAPER  180

Human  180   VASLSRVCVPLITLTDVDPLVEALLICHGREPQEILQPEFFEAVNEAILLKKISLPMSAV  239
             + SLS VCVPL+TL D++PLVEALL  HG EPQE+L PEFFEAVNEA L +KI LP S+V
Mouse  181   MMSLSEVCVPLVTLPDMEPLVEALLTYHGHEPQEVLAPEFFEAVNEAFLSEKIVLPTSSV  240

Human  240   VCLWLRHLPSLEKAMLHLFEKLISSERNCLRRIECFIKDSSLPQAACHPAIFRVVDEMFR  299
             V LW RHLPSLEKA LHLFEKL SS+  CLRR+EC I++S LPQAAC PAIFR+VDEMFR
Mouse  241   VSLWFRHLPSLEKATLHLFEKLFSSKIICLRRMECCIRESFLPQAACQPAIFRIVDEMFR  300

Human  300   CALLETDGALEIIATIQVFTQCFVEALEKASKQLRFALKTYFPYTSPSLAMVLLQDPQDI  359
               LLETDGA E++A +QVFT C VEAL+K +KQL FAL+TYFPY +P LA  L Q P+ I
Mouse  301   FVLLETDGAPEVLAALQVFTSCLVEALKKENKQLTFALRTYFPYGAPCLAAALSQHPEAI  360

Human  360   PRGHWLQTLKHISELLREAVEDQTHGSCGGPFESWFLFIHFGGWAEM-VAEQLLMSAAEP  418
             P+GH LQ L HIS+LLREAVED T GS   PFESWFLF+HFGGW ++ VAE LL   AEP
Mouse  361   PQGHRLQPLLHISQLLREAVEDCTRGSPRNPFESWFLFVHFGGWVDLAVAELLLREEAEP  420

Human  419   PTALLWLLAFYYGPRDGRQQRAQTMVQVKAVLGHLLAMSRSSSLSAQDLQTVAGQGTDTD  478
             P  LLWLL FYY P+DG QQR Q+MV++K ++  LL + RS  LSA DLQ  A +    D
Mouse  421   PAGLLWLLVFYYSPQDGSQQREQSMVELKVLINRLLMLLRSGPLSATDLQE-AAESPSGD  479

Human  479   LRAPA-QQLIRHLLLNFLLWAPGGHTIAWDVITLMAHTAEITHEIIGFLDQTLYRWNRLG  537
              R P   QL+R LLL+ LLW P GH I W+ +T MAHT  + HEIIGFLDQTLYR   L
Mouse  480   PRPPVCGQLVRRLLLSLLLWTPEGHAIVWEAVTHMAHTDAVIHEIIGFLDQTLYRSQHLC  539

Human  538   IESPRSEKLARELLKELRTQV  558
             +E+ R  KLAR+LLKEL+ QV
Mouse  540   VEASR--KLARDLLKELQAQV  558
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Figure S4. Alignment of human and murine FANCC/Fancc amino acid sequences

Sequences obtained from the National Center for Biotechnology Information's (NCBI) Protein Database and were aligned using the NCBI Blast program. Identical residues are listed as characters in the lines of text between the given human and murine sequences. Each blank space between the human and mouse sequences means that the residues do not match. A plus sign (+) denotes conserved residues.

Cell culture conditions. Cells were grown in alpha-Minimal Essential Medium (primary fibroblasts), Dulbecco's Modified Eagle Medium (transformed MEFs and tongue epithelial cells), or Iscove's Modified Dulbecco's Medium (hematopoietic progenitors; IMDM). All media were purchased from Invitrogen. Fibroblasts and epithelial cells were grown in 10% fetal bovine serum (Hyclone) and treated with and without MMC (Sigma-Aldrich) for 5 days. Hematopoietic progenitors were grown in 5% fetal calf serum (FCS; Hyclone) and clonogenic growth assays were performed in 1% IMDM methylcellulose (Stem Cell Technology) with 30% fetal calf serum (Hyclone) and mIL-6 (200u/mL) and mSCF (100 ng/mL; both from Peprotech).

***mFancc* cloning.** Total RNA was prepared from the liver of a wild-type C57Bl/6J mouse. *mFancc* cDNA was amplified by PCR with the following primers (containing Hpa1 sites): mFAC-forward (5′ ATG GCT CAG GAG TCT GCA GAC CTT GCT TCT GAC 3′) and mFAC-reverse (5′ CTA GAC CTG GGC TTG CAG CTC CTT TAG GAG GTC 4′). The resulting product was sub-cloned into the TOPO TA Cloning Kit (Invitrogen), digested with Hpa 1 restriction enzyme (Invitrogen) and sub-cloned into pLXSH. All plasmids were sequenced with a primer directed against the 5' pLXSH sequence and an internal sequence primer at the OHSU Sequencing Core Facility.

Gene transduction. pL-*mFancc*-SH and pL-*hFANCC*-SH were transfected into Ψ -2 or PA-12 cells (the packaging cell line). Virions were collected and used to transduce MEFs and epithelial cells. For hematopoietic cells, *mFancc* and *hFANCC* were sub-cloned into the foamy virus MD9-GFP vector and transfected into 293T cells.[17] Virions

were collected and used to transduce freshly isolated hematopoietic progenitors. Transduction efficiencies of hematopoietic progenitors were calculated after colony formation by measuring the percentage of GFP-positive colonies by PCR.

RNA isolation and real-time PCR. Total RNA was prepared from 1-5 $\times 10^6$ cells using the RNeasy Mini kit (Qiagen, Valencia, CA, USA). Complementary DNA synthesis and real-time PCR were performed as described previously[14]. Predesigned primer and probe sets for *mFancc* (Mm00514846_m1) and *hFANCC* (Hs00164592_m1) were purchased as Taqman Gene Expression Assays and probe/primer sets for pLSXH sequences (used for comparative measurements of transduced *mFancc* and *hFANCC* levels in MEFs) were designed and ordered from Applied Biosystems. pLXSH primers were: PSIsig5' (5'-GAA TTT TTG CTT TCG GTT TGG A-3' and PSIsig3' (5'-CAG CGC TGC AGC AGA CAA-3').