**Supplementary Table 1:** A summary ofzebrafish cancer predisposition syndrome models, specifying CPGs involved, zebrafish strains, and associated phenotypes. dpf = days post-fertilization.

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| --- | --- | --- | --- | --- | --- | --- |
| **Cancer Predisposition Syndrome** | **CPG** | **Zebrafish Model** | **Tumor Types** | **Associated Phenotypes** | **Method** | **References** |
| Li-Fraumeni Syndrome | *TP53* | *tp53*N168K | Not reported | Resistant to apoptosisfollowing induction of DNA damage only at 37ºC | ENU | (Berghmans et al., 2005) |
| *tp53*M214K | MPNSTs | Resistant to apoptosis following induction of DNA damage | ENU |
| *tp53*I166T | Sarcomas | ENU | (Parant et al., 2010) |
| *tp53*-/- | MPNSTs, angiosarcomas, germ cell tumors, a natural killer cell-like leukemia | TALEN | (Ignatius et al., 2018) |
| *tp53*R217H | Not yet characterized | Not yet characterized | CRISPR | (Prykhozhij et al., 2018b) |
| Familial Adenomatous Polyposis | *APC* | *apc*MCR/MCR | Intestinal adenomas in heterozygotes | Cardiac valve defect, curved body types, lack colonocyte differentiation, do not survive past 15dpf | ENU | (Hurlstone et al., 2003; Nadauld et al., 2005; Haramis et al., 2006) |
| Peutz-Jeghers Syndrome | *LKB1* | *lkb1-/-* | Not reported | Starvation phenotype that causes lethality by 7-8 dpf, metabolic state resembles aerobic glycolysis | ENU | (Van Der Velden et al., 2011) |
| Cowden Syndrome | *PTEN* | *ptenb­-/-* | Neuroepitheliomas | Phenotypically normal | ENU | (Faucherre et al., 2008) |
| *ptena*-/-; *ptenb*+/- | Hemangiosarcomas near the eye | 10% tumor incidence | ENU | (Choorapoikayil et al., 2012) |
| *ptena*+/-; *ptenb*-/- | 2% tumor incidence | Breeding |
| *ptena-*/-; *ptenb*-/- | Not reported | Enhanced angiogenesis, lethal by 5dpf | Breeding | (Choorapoikayil et al., 2013) |
| Tuberous Sclerosis Complex | *TSC2* | *tsc2*vu242/vu242 | Not reported | Increased mTORC1 but lethal by 11dpf | ENU | (Kim et al., 2011) |
| *tsc2*vu242/+; *tp53*M214K/M214K | Multiple malignancies | Increased mTORC1 and angiogenesis | Breeding | (Kim et al., 2013) |
| Noonan/LEOPARD Syndrome | *PTPN11* | *ptpn11b*-/- | Not reported | Phenotypically normal | ENU | (Bonetti et al., 2014b) |
| *ptpn11a-/-* | Cardiac and pleotropic defects, lethal by 5dpf | ENU |
| *ptpn11a*-/-; *ptpn11b*-/- | Breeding |
| *c-CBL* Mutation Associated Syndrome | *c-CBL* | *c-cbl*H382Y | Not reported | Myeloproliferative phenotype, median survival of 15dpf | ENU | (Peng et al., 2015) |
| Costello Syndrome | *HRAS* | *HRAS*G12V | Melanomas, gut carcinomas, hepatocarcinomas, rhabdomyosarcoma | Traits of Costello syndrome | Transgene | (Santoriello et al., 2009) |
| Neurofibromatosis Type 1 | *NF1* | *nf1a*-/-; *nf1b*-/- | Not reported | Nervous system defects, melanophore phenotype, do not survive past 10dpf | ZFN | (Shin et al., 2012) |
| *nf1a*+/-; *nf1b*-/-; *tp53M214K/M214K* | High-grade gliomas and MPNSTs | Increased onset and penetrance of tumor development | Breeding |
| *nf1a*+/-; *nf1b*-/-; *tp53M214K/M214K; sox10:PDGFRA*WT | MPNSTs | Nervous system defects, melanophore phenotype,decreased time to tumor onset | Breeding, Transgene | (Ki et al., 2017) |
| Dyskeratosis Congenita | *TERT* | *tert*-/- | Not reported | Premature aging, reduced telomere length, decreased fertility, shortened lifespans | ENU | (Anchelin et al., 2013) |
| *NOP10* | hi2578 | Not reported | Fail to form HSCs, ribosomal defects, cytopenia | Retroviral insertion | (Pereboom et al., 2011) |
| Shwachman-Diamond Syndrome | *SDBS* | *sbdsnu16* | Not reported | Growth defects, pancreatic atrophy after 15dpf, do not survive past 21dpf | CRISPR | (Oyarbide et al., 2020) |
| *sbdsnu132* | Neutropenia, growth defects, pancreatic atrophy after 15dpf, do not survive past 21dpf | CRISPR |
| Wiskott-Aldrich Syndrome and X-linked Congenital Neutropenia | *WASp* | *wasp1*-/- | Not reported | Impaired immune response | ENU | (Jones et al., 2013) |
| *wasp1*-/-; hWASp | Rescues neutrophil response to a wound site | Breeding, Transgene |
| *wasp1*-/-; hWASpI294T | Neutropenia | Breeding, Transgene |
| *wasp1*-/-; hWASpH246D | Rescued cell motility and recruitment | Breeding, Transgene |
| *wasp1*-/-; hWASpY291F | Slight improvement for neutrophil migration | Breeding, Transgene |
| *wasp1*-/-; hWASpI294T | Hyperprotrusive neutrophils with increased velocity during wound response | Breeding, Transgene |
| GATA2 Deficiency Syndromes | *GATA2* | *gata2aΔi4/Δi4* | Not reported | Decreased blood cells in kidney marrow, immune and lymphatic defects similar to GATA2 deficiency syndromes | CRISPR | (Dobrzycki et al., 2020) |
| *gata2b*+/- | Reduced myeloid differentiation and dysplastic myeloid cells in adults | CRISPR | (Avagyan et al., 2017; Gioacchino et al., 2019) |
| Familial AML | *CEBPA* | *molihkz7* | Not reported | Defects in myeloid progenitor proliferation & differentiation | ENU | (Dai et al., 2016) |
| *cebpasum2* | TALEN |
| *cebpasum3* | TALEN |
| *cebpa*Cterm/Nterm | Leukemic transformation between 4-6 weeks of age | Defects in mature myelocytes and monocytes | TALEN | (Hockings et al., 2018) |
| *cebpa*Nterm/Nterm | TALEN |
| Familial Platelet Disorder with Predisposition to AML | *RUNX1* | *runx1*W84X/W84X | Not reported | Reduced number of neutrophils, thrombocytes, and B-cells | ENU | (Sood et al., 2010; Jin et al., 2012; Chi et al., 2018) |
| Congenital Amegakaryocytic Thrombocytopenia | *MPL* | *mpl*smu3 | Not reported | Severe thrombocytopenia, reduced homeostasis and abnormal bleeding | TALEN | (Lin et al., 2017) |
| Fanconi Anemia | *FANCA* | *fanca*\_hg41 | Not reported | Female-to-male sex reversal | CRISPR | (Ramanagoudr-Bhojappa et al., 2018) |
| *FANCB* | *fancb*\_hg42 | CRISPR |
| *FANCC* | *fancc*\_hg43 | CRISPR |
| *FANCD2* | *fancd2*\_hg47 | CRISPR |
| *FANCE* | *fance\_hg48* | CRISPR |
| *FANCF* | *fancf\_hg50* | CRISPR |
| *FANCG* | *fancg\_hg53* | CRISPR |
| *FANCI* | *fanci\_hg54* | CRISPR |
| *FANCJ/ BRIP1* | *fancj\_hg56* | CRISPR |
| *FANCJ/ BRIP1* | *fancj\_hg57* | CRISPR |
| *FANCL* | *fancl\_hg59* | CRISPR |
| *FANCM* | *fancm\_hg60* | CRISPR |
| *FANCN/ PALB2* | *fancn\_hg62* | CRISPR |
| *FANCO/ RAD51C* | *fanco\_hg65* | CRISPR |
| *FANCP/ SLX4* | *fancp\_hg66* | CRISPR |
| *FANCT/ UBE2T* | *fanct\_hg70* | CRISPR |
| *FAAP24* | *faap24* | CRISPR |
| *FAAP100* | *faap100* | CRISPR |
| *FANCD1/BRCA2* | *fancd1*\_hg45 | CRISPR |
| *brca2*Q658X/Q658X | Testicular neoplasia | Female-to-male sex reversal | ENU | (Shive et al., 2010) |
| *brca2*Q658X/Q658X; tp53+/M214K | MPNSTs, sarcomas, nephroblastomas | Accelerated tumorigenesis | Breeding | (Shive et al., 2010, 2014) |
| *brca2*-/- | Testicular neoplasia | Female-to-male sex reversal, genome instability, male sterility | Retroviral insertion | (Rodríguez-Marí et al., 2011) |
| *brca2-/-; tp53*M214K/M214K | Testicular and invasive ovarian tumours | Rescued ovarian development but females were sterile, male sterility, reduced apoptosis, accelerated tumorigenesis | Breeding |
| *zeppelin* | Not reported | Defects in kidney development, interrenal gland expansion | ENU | (Kroeger et al., 2017) |
| *FANCR/ RAD51* | *rad51*-/- | Not reported | Female-to-male sex reversal, increased chromosomal aberrations following induction of DNA damage, size defects, decreased blood cells in adult kidney marrow | ENU | (Botthof et al., 2017) |
| *rad51*-/-; *tp53*M214K/M214K | MPNSTs | Rescued HSPC defects and sex reversal, adult sterility, size defects, decreased time to tumor onset compared to *tp53* mutants | Breeding |
| CPGs not associated with a cancer predisposition syndrome | *MLH1* | *mlh1*-/- | Neurofibromas, MPNSTs, PNETs, hemangiosarcomas | Males are infertile with abnormal testis histology, females are fertile but produce triploid embryos | ENU | (Feitsma et al., 2007, 2008; Leal et al., 2008) |
| *MSH2* | *msh2*-/- | Microsatellite instability in mutant male progeny | ENU | (Feitsma et al., 2008) |
| *MSH6* | *msh6*-/- | ENU |
| *ATRX* | *atrx*-/- | None | Do not survive past larvae stages, erythrocytes are more spherical | CRISPR | (Oppel et al., 2019) |
| *tp53*M214K/M214K*;nf1b-/-;nf1a+/-;atrx+/-* | Epithelioid sarcomas, angiosarcomas, and rare carcinomas | Wider spectrum of tumor types, lengthening of telomeres | Breeding |
| *VHL* | *vhl-/-*; *vll-/-* | None | Resistant to apoptosis following induction of DNA damage, upregulation of HIF target genes, slowed growth, reduced consumption of yolk | ENU (*vhl*)ZFN (*vll*) | (Kim et al., 2020) |