Supplementary Table 1: Known human polymorphisms for efficacy and toxicity of chemotherapy drugs

Carboplatin	
Polymorphism	**Description**
ALDH3A1*2	This mutation increases the risk of haemorrhagic cystitis with carboplatin treatment [20].
ALDH1A1*2	This mutation increases the risk of liver toxicity with carboplatin treatment [20].
ERCC1 C8092A	In carboplatin treatment of non-small cell lung cancer, this mutation has a significant association with higher toxicity [21]. This result was not confirmed by Booton *et al.* [22]
ERCC1 T118C	Homozygous TT patients have a better response to carboplatin treatment than heterozygotes or homozygous CC patients [23]. This result was not confirmed by Booton *et al.* [22]
ERCC2 A35931C	In carboplatin treatment of non-small cell lung cancer, this mutation has a significant association with higher toxicity [21].
GSTP1 A342G	Patients with this mutation were more sensitive to carboplatin treatment [24].
hMSH2 TgIVS12-6C	Patients with the homozygous CC genotyped responded significantly better to carboplatin treatment. No significant effect was observed for heterozygous patients [25].
hMLH1 T1151A	No significant response difference to carboplatin treatment was observed for this polymorphism [25].
MRP2 C24T	Patients with this mutation were more sensitive to carboplatin treatment [24].
Floxuridine	
Polymorphism	**Description**
CDA A79C	In patients with this mutation there was a 19% decrease in plasma clearance of floxuridine [26].
CDA G208A	This mutation was associated with 64% lowered plasma clearance of floxuridine in homozygotes and 17% lowered clearance in heterozygotes [26].
CDA -31delC	A 7% decrease in plasma clearance was observed for this deletion [26].
MTHFR A1298C	A significantly higher efficacy of floxuridine was observed with the CC genotype [27].
TS Y33H	This mutation is associated with a four-fold resistance to floxuridine [28].
TYMS 2R 3Rc 3Rg	A higher number of tandem repeats on the TYMS gene is associated with higher floxuridine efficacy [29].
Gemcitabine (GEM)	

Polymorphism	Description
CDA A76C	This mutation was significantly associated with neutropenia toxicity and decreased efficacy post gemcitabine hydrochloride treatment in patients with locally advanced pancreatic cancer [30]. Another study confirms that gemcitabine efficacy was lowered due to this mutation [31]. However, the gene was not found to have significant impact on gemcitabine pharmacokinetics in non-small-cell lung cancer (NSCLC) patients [32].
CDA G208A	In a study of 250 Japanese cancer patients Suguyama et al. observed that there was an effect of this mutation on the plasma clearance rate of GEM [33]. Yonemori *et al*. show that patients homozygous for the mutation experienced significantly higher toxicity with gemcitabine than other patients [34]. Ueno et al. confirmed the toxicity associated with this mutation [35].
dCK C-1205T	This mutation was significantly associated with lowered tumor response to gemcitabine-based therapy and was marginally associated with progression-free survival [30].
dCK A 9846G	Homozygotes for this mutation were shown to be less sensitive to gemcitabine compared with heterozygotes and homozygous wild-type patients when treated for pancreatic cancer [36].
hCNT1 G565A	Patients heterozygous and homozygous for the mutation show lower GEM plasma clearance for treatment of solid tumors than patients without the mutation [37].
hENT1 A-201G	This mutation was significantly associated with lowered tumor response to gemcitabine-based therapy and was marginally associated with progression-free survival [30].
hENT1 G-706C	Homozygous patients without this mutation have 10% higher plasma clearance of GEM when treated for solid tumor cancers [37].
hENT1 C913T	This mutation was significantly associated with neutropenia toxicity post gemcitabine hydrochloride treatment in patients with locally advanced pancreatic cancer [30].
MRP2 G40A	This mutation was associated with lowered efficacy in preoperative gemcitabine treatment [38].
MTHFR C677T	In the CC genotype gemcitabine was significantly more efficacious than in CT and TT genotypes [39].
RRM1 A33G	This mutation was significantly associated with lowered tumor response to gemcitabine-based therapy and was marginally associated with progression-free survival [30].
SMYD3	SMYD3 knock-down lowered the efficacy of gemcitabine in treatment of pancreatic cancer [40].

Methotrexate (MTX)	
Polymorphism	**Description**
ABCC2 C-24T	The risk to have folinate rescue as 9-fold in female patients carrying at least one -24T allele [41].
AMPD1 C34T	Patients with the T variant were more likely to have a good clinical response to MTX treatment [42].
ATIC C347G	Patients with the 347CC genotype were more likely to have a good clinical response to MTX treatment [42].
ITPA C94A	Patients with the 94CC genotype were more likely to have a good clinical response to MTX treatment [42].
MTHFR C677T	Better response to MTX treatment, but higher toxicity [43]. Patients homozygous for the mutation had significantly lowered plasma clearance of MTX [44]. The T variant was associated with a significantly higher frequency of rheumatoid arthritis remission [45]. Seidemann et al. found that this polymorphism does not appear to influence the outcome or therapy-associate toxicity in pediatric patients with non-Hodgkin's lymphoma (NHL) treated with high-dose methotrexate infusion regimens [46].
MTHFR A1298C	Patients homozygous for the variant were at decreased risk for leucopenia [44]. The C variant was associated with a significantly higher frequency of rheumatoid arthritis (RA) remission [45]. The 1298A variant was associated with MTX-related adverse events in Caucasians [47].
MTHFR A80G	Patients homozygous for the variant were at decreased risk for leucopenia [44].
RFC-1 G80A	The frequency of the AA genotype was higher among MTX responders compared to poor MTX responders in RA treatment [48].
Mitomycin C (MMC)	
Polymorphism	**Description**
NQO1 C609T	A C>T mutation in the NQO1 gene at the 609 position was shown to lower the expression of the DT-diaphorase enzyme, which is thought to be involved in MMC efficacy [49]. Some studies show that the efficacy of MMC in ovarian and bladder tumors of patients with the mutation was significantly lowered [50], while another study did not confirm this result in bladder cancer [51]. Lowered MMC efficacy was also not confirmed for colon cancer [52] and metastatic breast cancer [53].
NQO1 T14055C	The efficacy of MMC in ovarian and bladder tumors of patients with this mutation was significantly

lowered [50].

Topotecan	
Polymorphism	**Description**
ABCG2 C914A	This mutation in the ABCG2 gene shows a 30% reduction in the efflux transporter [54]. A study shows increased toxicity in heterozygous and homozygous mutant patients [55].
MDR1 G1199T	This mutation was not correlated with efficacy reduction when topotecan was used for kidney cancer treatment [56].

Supplementary Table 2: Chemotherapeutic Agents

Dose-Response and consistent knock-down in heritability treatment

Name	Class	Uses
Carboplatin	Alkylating Agent	Ovarian carcinoma, lung, head and neck cancers
Floxuridine	Antimetabolite	Colorectal cancer
Gemcitabine Hydrochloride	Antimetabolite	Non-small cell lung cancer, pancreatic cancer, bladder cancer and breast cancer.
Methotrexate	Antimetabolite	Acute lymphoblastic leukemia
Mitomycin C	Antibiotic	Upper gastro-intestinal (e.g. esophageal carcinoma) and breast cancers, as well as by bladder instillation for superficial bladder tumors
Topotecan	Topoisomerase I Inhibitor	Ovarian cancer and lung cancer

Insoluble[1]

Name	Class	Uses
Cladribine	Antimetabolite	Hairy cell leukemia, chronic lymphocytic leukemia, nonHodgkin's lymphomas
Docetaxel	Plant Alkaloid, taxane, antimicrotubule agent	Breast Cancer, non-small cell lung cancer, advanced stomach cancer, head and neck cancer, and metastatic prostate cancer
Etoposide	Plant Alkaloid, topoismerase II inhibitor	Testicular, bladder, prostate, lung, stomach, and uterine, cancers. Hodgkin's and non-Hodgkin's lymphoma, mycosis fungoides, Kaposi's sarcoma, Wilm's tumor, rhabdomyosarcoma, Ewing's sarcoma, neuroblastoma, brain tumors
Paclitaxel	Plant Alkaloid, taxane, antimicrotubule agent	breast, ovarian, lung, bladder, prostate, melanoma, esophageal, as well as other types of solid tumor cancers
Tamoxifen	Anti-estrogen	Metastatic breast cancer, ovarian cancer

Fatal at Working Dose[2]

Name	Class	Uses

Doxorubicin	Anthracycline antibiotic	Bladder, breast, head and neck, leukemia (some types), liver, lung, lymphomas, mesothelioma, multiple myeloma, neuroblastoma, ovary, pancreas, prostate, sarcomas, stomach, testis (germ cell), thyroid, and uterus cancers

No Female Fertility Response to Varied Doses[3]

Name	Class	Uses
5-Fluorouracil	Antimetabolite	Colon, rectal, breast, gastrointestinal, head and neck, and ovarian cancer
6-Mercaptopurine	Antimetabolite	Acute lymphoblastic leukemia
Cisplatin	Alkylating agent	Testicular, ovarian, bladder, head and neck, esophageal, small and non-small cell lung, breast, cervical, stomach and prostate cancers
Cytarabine	Antimetabolite	Different forms of leukemia, lymphoma
Mitoxantrone	Antitumor Antibiotic	Advanced prostate cancer, acute myelogenous leukemia, breast cancer, non-Hodgkin's lymphoma
Procarbazine	Alkylating agent	Hodgkin's disease, non-Hodgkin's lymphoma, brain tumors, melanoma, lung cancer, and multiple myeloma
Vinorelbine	Plant alkaloid	Non-small lung cancer, breast cancer, ovarian cancer, Hodgkin's disease

1. Because chemotherapy is delivered orally with food to flies in our assay, we are unable to deliver drugs that are not easily soluble in water, or ones that come out of solution.
2. The three drugs listed under this category were not used in our heritability assay because they were fatal to the treated females without a significant reduction in fertility.
3. Maximum dose was set at 150mM. If the chemotherapy agent had to effect on the female fecundity at this dose, it was not used in the heritability assay.

Supplementary Table 3: Liquid Food Recipe

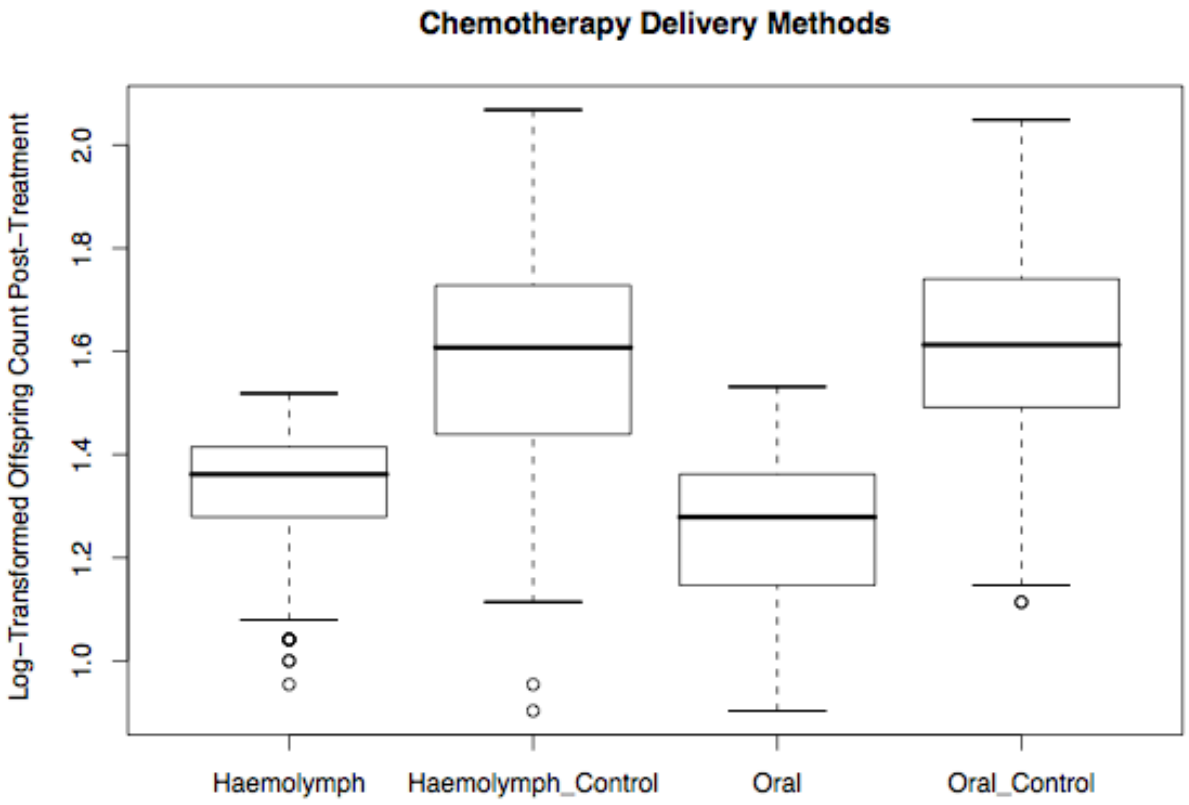
Ingredient	Amount[1]
Sucrose	12.5 g
Active Dry Yeast – Fisher Cat#: 8013-01-2	17.5 g
Corn Syrup (light) – Karo®	5 ml
PBS	95 ml

1. For a total of 100 ml – autoclaved after mixing

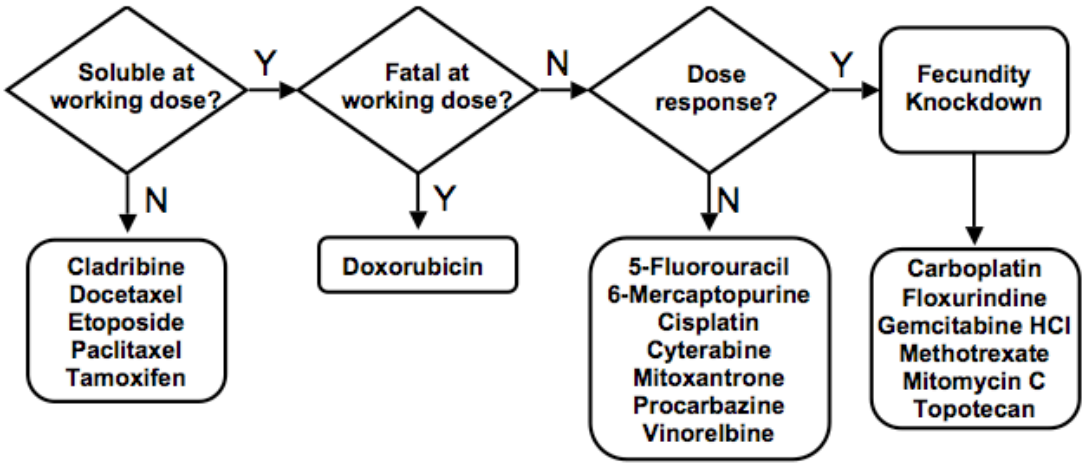
Supplementary Table 4: Recovery and "lay-out" Fly Food

Ingredient	Amount[1]
Water	78.4 ml
Agar	0.84 g
Dextrose	6.31 g
Sucrose	3.423 g
K, Na Tartrate	0.96 g
calcium chloride	0.07 g
corn meal	7.6 g
Yeast suspension	
-yeast	3.2 g
-water	20 ml
Propionic acid	1.6 ml
Tegosept	
-tegosept	0.1 g
-ethanol	1 ml

1. For a total of 100 ml



Supplementary Figure 1 – Results of drug delivery experiment. Methotrexate was delivered at a 1.5mM concentration to *D. melanogaster* in two forms: oral mixture in liquid food (Supplementary Table 3) and via haemolymph injections [16]. Two hundred flies were treated with methotrexate and their offspring were counted as a measure of toxicity – the y-axis represents $\log_{10}$ – transformed number of offspring produced by each female post-chemotherapeutic agent treatment. The F-test, which tests for the difference of two variances for a sample size of 200 in each group, showed that the variances of the two groups were statistically similar ($p>0.07$).



Supplementary Figure 2 – Chemotherapeutic agents. This figure demonstrates the steps taken to arrive at the final chemotherapeutic agents used in our heritability assay. Some of the drugs were not soluble in water, and we were unable to deliver them orally to flies, of those that were soluble, Doxorubicin was fatal to Drosophila. Seven of the drugs did not have a significant reduction in female fecundity at different doses delivered. Six of the drugs we tested had a statistically significant dose response (see also Figure 1).