

# WuXi AppTec Customized Formula Diet Platform



WuXi AppTec, WuXi Biology, Oncology & Immunology Unit



## WuXi AppTec Customized Formula Diet Platform



**Formula diet-influenced tumor model solution**



**Formula diet-controlled disease model solution**



**Formula diet-treated tumor model solution**

- Feed is the only food source for experimental animals, and has a profound impact on animals. By changing the type, composition, and quantity of feed, different experimental purposes can be achieved, such as diet-induced disease models, diet administration.
- WuXi AppTec's customized diet research platform provides you with multiple validated diet related models.



# Formula diet-influenced tumor model solution

Nutrients diet, chemical diet related tumor biology



**Formula diet-influenced tumor model solution**

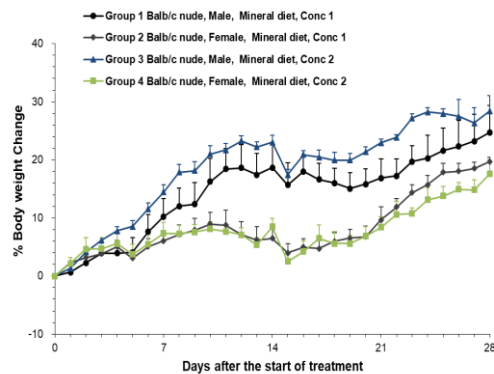


Formula diet-controlled disease model solution

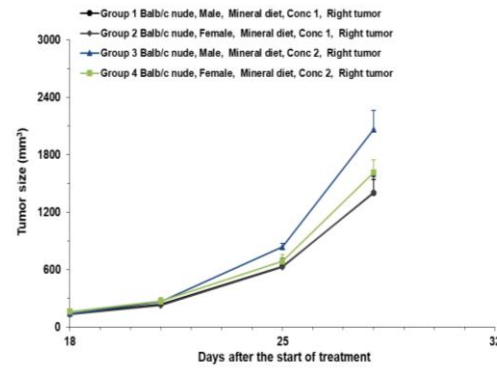


Formula diet-treated tumor model solution

**A** Body weight change under mineral A formula

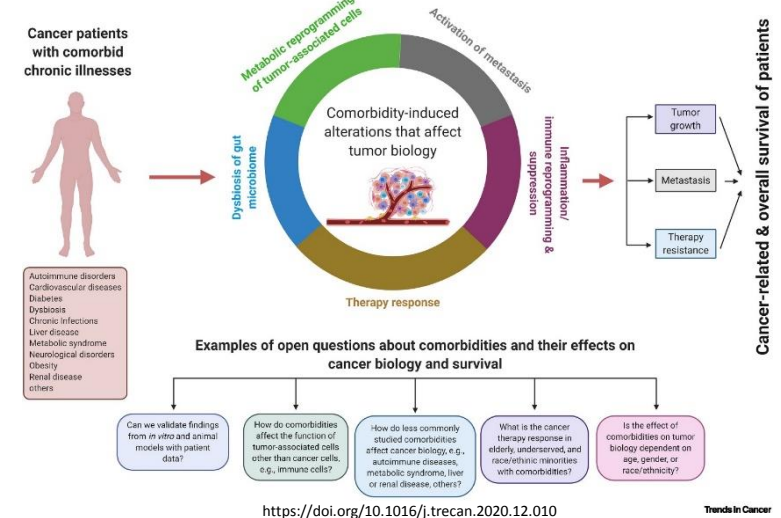


**B** Tumor growth under mineral A formula



**Figure.** Mineral A has been reported to have a certain inhibitory effect on tumor growth, which is not contained in normal mouse diets **A**. Under the feeding of mineral A diet, the mice maintained healthy body condition and gained steady weight. **B**. Tumor growth was also slightly inhibited by feeding with mineral A diet

- Nutrients like carbohydrates, fat and oil, minerals, and proteins in diet influence tumor biology and thus directly or indirectly affect tumor treatment and prognosis.
- To evaluate drug or treatment efficacy on tumor with comorbidities, we apply different animal diet at the same time as tumor inoculation to establish tumor comorbidity models.
- We provide all kinds of customized and commercial diets, like high-fat diet, high-sucrose diet, and mineral diets.



# Formula diet-controlled disease model solution

Introduction of Tet-Off and Tet-On gene expression systems



Formula diet-influenced tumor model solution



**Formula diet-controlled disease model solution**




Formula diet-treated tumor model solution

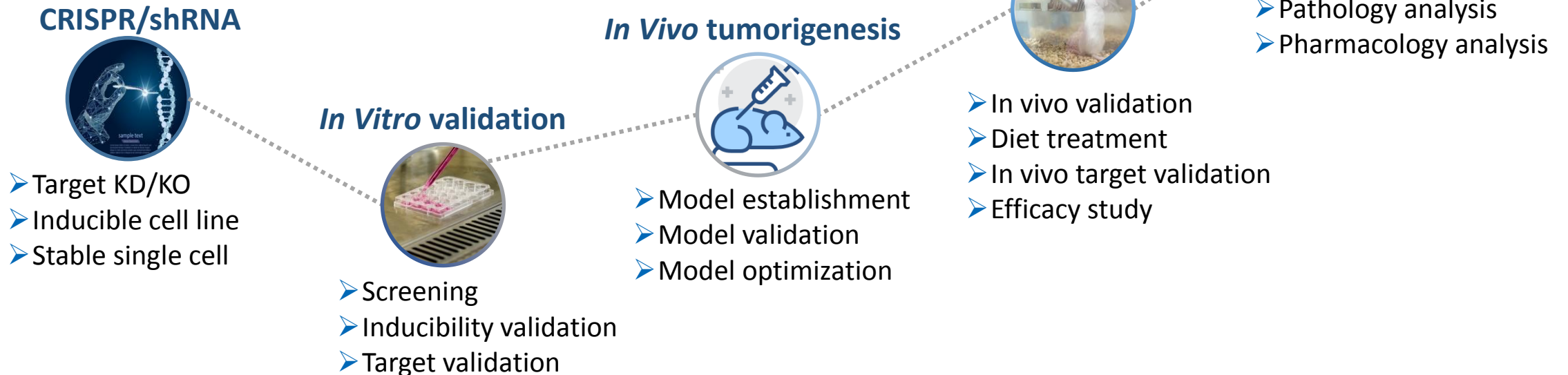


<https://www.addgene.org/>  
<https://www.takarabio.com/>

- The Tet-Off and Tet-On gene expression systems are extremely tight on/off regulated systems, with high inducibility, fast response time, and high absolute expression levels. In the Tet Off system, gene expression is turned on when doxycycline (Dox) is removed. In contrast, expression is turned on in the Tet-On system by the addition of Dox.
- In order to better support validate targets and evaluate drug efficacy, we have established a set of in vivo tumor models controlled by Dox diet to provide you with full-process services from engineering cell lines to sample analysis.

## Dox diet-induced target gene knockdown/knockout model solution

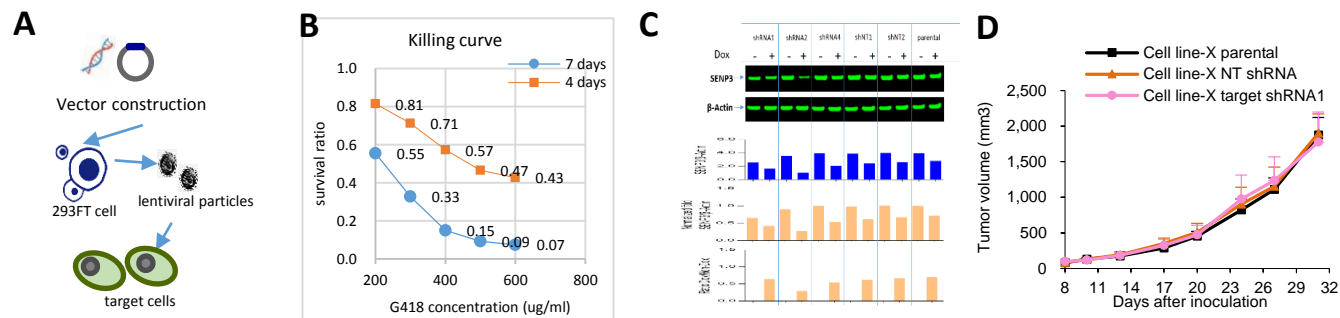
 We provide a package of Dox diet-induced system from the construction of inducible cell lines with CRISPR, *in vitro* and *in vivo* target validation and efficacy services, and *ex vivo* detection and analyses.



# Formula diet-controlled disease model solution

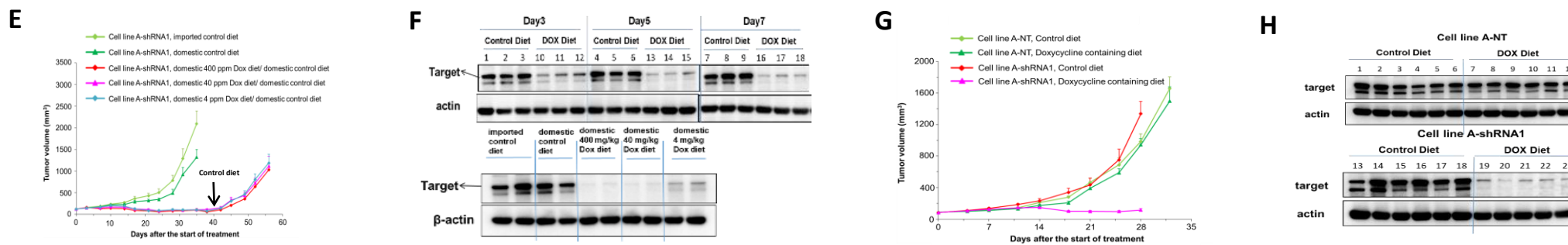
Case study: Dox diet-induced target gene KD tumor pharmacology study

Illustration of Dox induced target gene knockdown cell construction.



Growth properties	Construction Difficulty	Cell Line We have constructed
Suspension	hard	K562-luc, Kasumi-1, KG-1, MOLM13
Adherent	easy	MDA-MB-231, A549, Miapaca-2, Cal-51, MCF-7, BT-20

*In vivo* target validation or efficacy study through Dox induced target gene knockdown in tumor

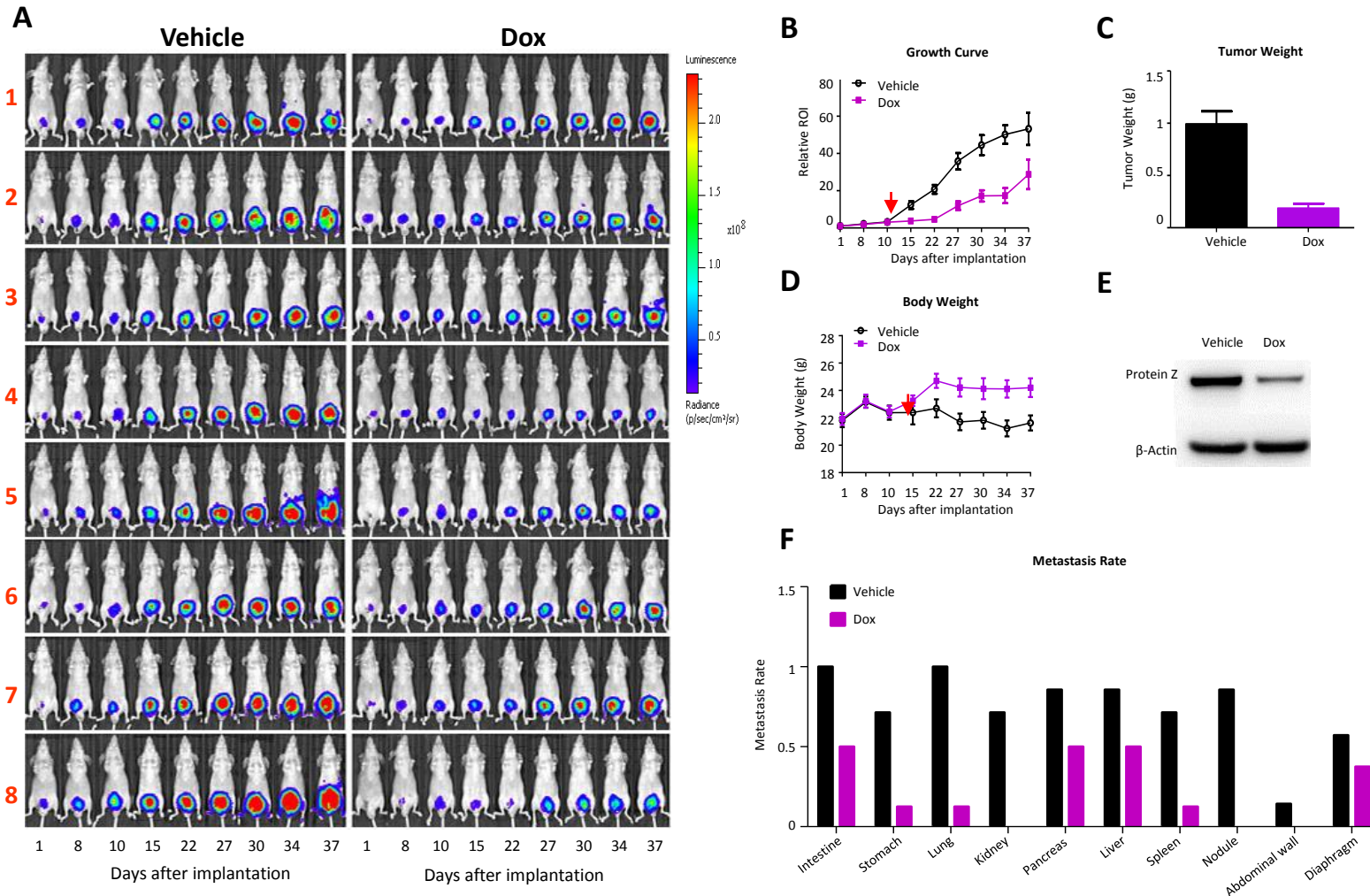


**Figure. A.** Dox-induced shRNA vectors were designed and transfected into 293FT cells to produce shRNA lentivirus. Target cells were infected and **B.** selected under pressure to obtain stable expression cell lines. **C.** Candidate cell lines were further validated by western blot to pick up a most potential cell line for *in vivo* study. **D.** The cells verified and selected *in vitro* were firstly subjected to tumorigenesis test to establish tumor models *in vivo*. **E.** The established model will then be tested for the induction of Dox gradient concentration to find an effective induction concentration. **F.** After verification *in vivo*, the efficacy of all concentration groups will be confirmed by western blot to see if the target protein expression is down regulated. **G.** Then the official efficacy study will be conducted and all the **H.** pharma dynamic assay like western blot will be performed.

# Formula diet-controlled disease model solution

Case study: Dox diet-induced target gene KD tumor pharmacology study

Efficacy of gene Z suppression on tumor growth of PC-3M-luc orthotopic model.



**Figure.** PC-3M-luc cells infected with indicated lentiviruses carrying indicated shRNAs were injected into prostate gland of Balb/c nude mice. The resultant mice were fed with 5% sucrose-containing drinking water containing 1mg/ml of doxycycline or not. **A.** Bioluminescent imaging of mice (n=8). **B.** Orthotopic tumor growth curve as measured by average relative photon intensity. Arrow indicates the start of dosing on day 10, when consecutive increase of photon intensity was observed. Significant tumor growth inhibition was observed in 1mg/mL Dox group as compared to corresponding vehicle group (p < 0.05). **C.** Average tumor weight of mice. **D.** Average bodyweight of mice. **E.** The expression of protein Z. **F.** The metastasis rate.

# Formula diet-treated tumor model solution

Client's lead compound-diet solution



Formula diet-influenced tumor model solution



Formula diet-controlled disease model solution



**Formula diet-treated tumor model solution**

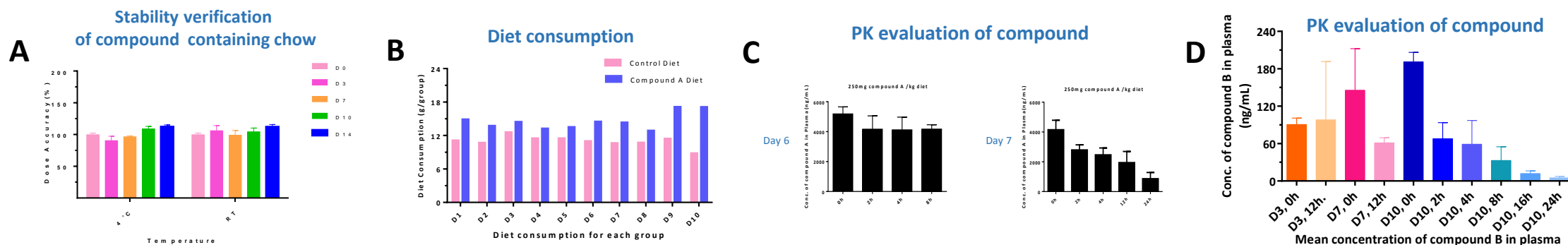
- Many lead compounds face a problem at early stage: **insoluble, fast metabolism, high toxicity compound**. Incorporate compound or special formula into experimental diet may help evaluate test article in vivo.
- Feeding test compounds can prevent dosing related stress and harm.
- Drug containing diets enable high concentration of drug in blood with a long period.
- Feeding test compounds can eliminate vehicle effects, and save time and labor.
- Customized formula diets are highly flexible to meet various demands.



# Formula diet-treated tumor model solution

Client's lead compound-diet solution

- For the client's lead compound, we start by making formula diet, compound dosage design and quality control, monitor intake and exposure.
- In the formal studies, the protocol will be adjusted as needed to ensure that the intake and exposure of the drug are falling in the target range



**Figure:** **A.** Accurate synthesis dose and formulated chow is stable at 4 ° C and RT. **B.** An appropriate proportion of the compound A diet will not affect the normal chow consumption of the mice, thus ensuring a stable compound A intake. **C.** During the formulated compound A chow treatment period (Day 0-6), the plasma exposure remained in a stable range, while the exposure showed time-dependent clearance after switching back to normal chow (Day 7). **D.** During the formulated compound B chow treatment period (Day 0-10), the plasma exposure remained in a certain range, while the exposure showed time-dependent clearance after switching back to normal chow (Day 10).



# OUR COMMITMENT

## *Improving Health. Making a Difference.*

For questions and requests, please email to [info\\_onco@wuxiapptec.com](mailto:info_onco@wuxiapptec.com)



<https://onco.wuxiapptec.com>