Selecting species for pharmaceutical and medical research

Letter to editor

Obtaining an approval either for a drug for a therapeutic use[1–4] or for biomedical equipment requires in the majority of cases laboratory experiments on cells and animals to describe the divers related details including the potential toxic effects, the side effects and the optimized conditions of use or administrations. Within this letter we aim to further illustrate how to select the species of animal to conduct the required tests on or to extract the cells, organs or molecules from those species that we need for *in vitro* tests and based on what a species is either included or excluded. Indeed, in some case such choice can be a struggle facing the development of the files since it depends on divers factors including the type of the conducted research, the investigated organ or system and the duration of the experiment. Therefore, clarifying the related concepts remains a priority for pharmaceutical and medical research.

The choice of animal species is also conditioned by the type of researches and on the organs we are willing to investigate. Indeed, some species are suitable for certain types or experiments[5] whereas others are not. Here in some illustrative examples are given. In neuroscience using monkeys, and due to the great similarity between them and humans, has allowed us to better understand the brain properties and the cognitive functions based on observations done on monkey's brains.[6,7] For the neural properties of the visual functions, cats represent a good choice since they have specific vision characteristics.[8–11] Furthermore, cats are also suitable for electrophysiological studies. Tree shrew, a species believed to be biologically between insectivore and primates with specific evolutionary properties,[12] is also used in neurobiological researches.[13–15] In addition to its low cost, its brain has a similar structure to the human brain. Mice[16,17] are commonly used due to their brains properties in term of neurobiological functions and the well tolerance they have towards the equipments used in recording. In genetics, due to their relatively simple genome and the short duration of life cycle, bacteria are used[18,19] to study the mutations and the gene interactions but the bacterial usage in genetics is limited. For instance, mammalians provide a better multi-cellular and multi-organs environment to study interactions between genes and cell signals. Moreover, results obtained with mammalians would be closer to the human profile than those obtained with bacterial studies. In pharmacology, for example when evaluating steroids, and since the steroids have specific blood transporters that transport also the endogenous steroid hormones, the animal selected for such study should have similar hormones to mimic the pharmacokinetic conditions.

For more precise or local studies we may use isolated parts of organs or even insects. Drosophila is an insect with a nervous system that include many of the human neurotransmitters which made this fly a suitable insect for neurobiological and neuropharmacological studies.[20–23] In addition, an animal's heart or kidney put within a physiological solution that mimics the physiological situation (temperature, ions concentrations, nutriment etc) may be an appropriate way to both study the physiology of the organ and eventually test

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some drugs, although these results may mainly give data about the pharmacodynamic aspects rather than pharmacokinetics. Importantly, the influence that chemicals used as reagents or media may influence the live cells and thus, the laboratory results[24,25] therefore the need for a negative control and condition optimization. *In vitro* cells culture is largely used in biological and pharmacological studies.[26] Herein the species form which we take cells is important and also depends on the test we are willing to conduct. It is known that for neurotoxicity cells we may use cell cultures derived from neuroblastoma of mammalians and for hepato-toxicity we can use culture liver cells. It is worth mentioning that the best options remain human cells since the results are more reliable in term of medical extrapolations.

The duration of experiments represent an important factor. For instance, a species with a short duration of life would not be suitable for drugs long-term effects evaluation or chronic toxicity tests but would be convenient for acute toxicity test. Furthermore, since the different life period of an animal will correspond to different factors and conditions such as cell membranes receptors expressions, intracellular biochemical activities and the neuro-signaling[27–34] which will have a strong impact on the pharmacological profile a study conducted on the animal, the short life duration will allow us to study the compounds (pharmakon or toxic agent[32]) effects depending on the animal age and life phases within a limited period of time. Within this context, embryonic development of Zebrafish is rapid, and its embryos are relatively large, robust, and transparent, and able to develop outside their mothers thus it is suitable for studies on embryos[35–39] such as the evaluation of drugs effects. In addition, Zebrafish has at the adult age a transparent body through which it is possible to visualize *in vivo* biological activities such as fluid metastasis and brain activities.

Other elements could be important such as the animal weight and depending on the concentration and the nature (drugs, toxic element[40] or natural products[40–45]) of the products we would inject into its body and the biocompatibility between the animal organs or the equipments we might implant within it body. Herein, more availability of data related to animals along with strong collaborations between experts including

zoologists, biologists and doctors represent one of the key elements required to further describe the ideal species for each experimental context. The species would be the one that has the maximum common properties with the humans within a defined context for the topics we are willing to investigate by taking into consideration the influencing factors and optimize the laboratory methods towards better results.

Furthermore, genetic similarities exist between Zebrafish and humans, which made them a model to study diseases such as leukemia and some other cancers. Importantly, genetically modifies animals, such as Cre-mutant mouse strains[46–48] represent an essential tool in biological and medical research. Indeed, family Alzheimer disease (FAD) genes are introduced to monkeys and mice brains through transgenic virus as one of the methods, among others,[49–53] used to obtain animals models of Alzheimer disease (AD)[29] used to study AD properties, pathogenesis, mechanisms and test therapeutic candidates. We conclude by emphasizing the importance of the species choice as the first step of optimizing the results of the related studies even before starting them and as the best way to ensure we can extrapolate our results and build further studies based on them.

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Conflict of interest

The author declares no conflict of interest.

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