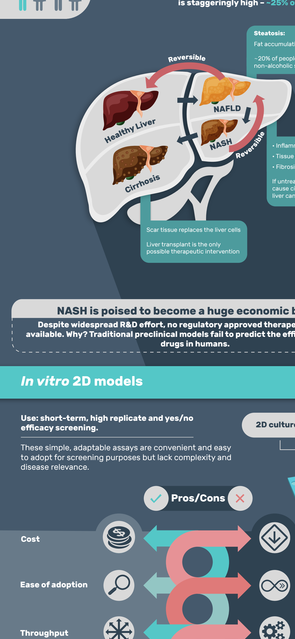
BioTechniques In Focus

CN-BIO

Pros and cons of preclinical models of non-alcoholic steatohepatitis

Non-alcoholic fatty liver disease (NALFD) is a spectrum of metabolic diseases linked to obesity and diabetes. Global prevalence of NAFLD is staggeringly high – ~25% of the population [1].



NASH is poised to become a huge economic burden.

Despite widespread R&D effort, no regulatory approved therapeutic drugs are available. Why? Traditional preclinical models fail to predict the efficacy of potential drugs in humans.

In vitro 2D models

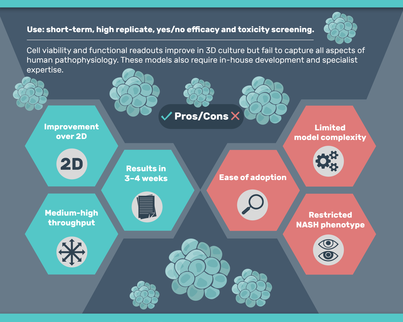
Use: short-term, high replicate and yes/no efficacy screening.

These simple, adaptable assays are convenient and easy to adopt for screening purposes but lack complexity and disease relevance.

In vitro 3D spheroid models

Use: short-term, high replicate, yes/no efficacy and toxicity screening.

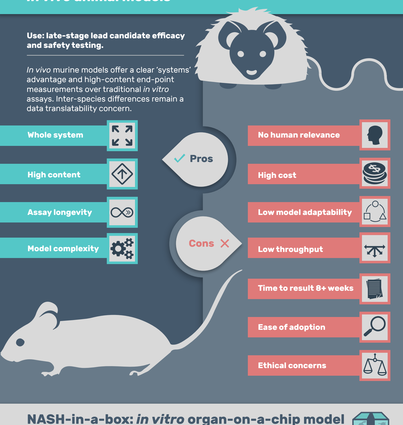
Cell viability and functional readouts improve in 3D culture but fail to capture all aspects of human pathophysiology. These models also require in-house development and specialist expertise.



In vivo animal models

Use: late-stage lead candidate efficacy and safety testing.

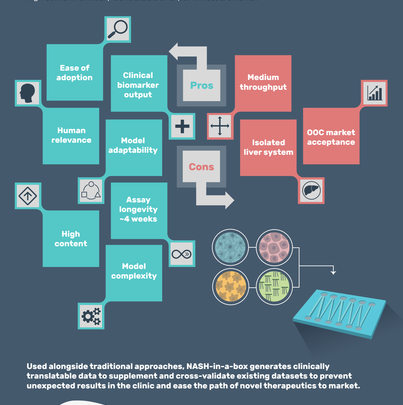
In vivo murine models offer a clear 'systems' advantage and high-content end-point measurements over traditional *in vitro* assays. Inter-species differences remain a data translatability concern.



NASH-in-a-box: *in vitro* organ-on-a-chip model

Use: target identification and validation, late-stage lead candidate efficacy and safety testing.

Organ-on-a-chip (OOC) NASH models exhibit advanced markers of inflammation, a robust fibrotic phenotype [2] and high content, clinically translatable end-point measurements.



Used alongside traditional approaches, NASH-in-a-box generates clinically translatable data to supplement and cross-validate existing datasets to prevent unexpected results in the clinic and ease the path of novel therapeutics to market.

Click here to find out more about NASH-in-a-box.

1 Chalasani N, Younossi Z, Lavine JE *et al.* The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 67(1), 328–57 (2018).

2 Kostrzewski T, Snow S, Lindström Battle A *et al.* Modelling human liver fibrosis in the context of non-alcoholic steatohepatitis using a microphysiological system. *Commun Biol.* 4(1), 1080 (2021).

This infographic has been created as part of a *BioTechniques* feature in association with CN Bio.

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