

Human tissue in drug discovery: promises and pitfalls

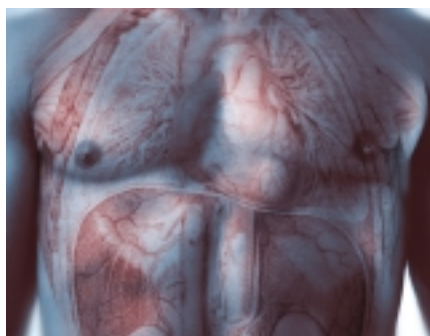
Katharine E. Barnes, BMN News

The use of human tissue in drug discovery shows promise in reducing the attrition rate of new drugs entering the clinic, say pharmacologists. But it demands new experimental approaches, validation and ethical consideration.

Smooth muscle tissue

Denis Crankshaw of McMaster University, Canada (<http://www.mcmaster.ca>) is using human smooth muscle tissue in lead optimization because he says smooth muscle is often the focus of a drug's side effects. For example, inappropriate contraction of airway smooth muscle leads to asthma, while inappropriate contraction of bladder smooth muscle can lead to urinary incontinence. Conversely, inappropriate relaxation of gastrointestinal smooth muscle can lead to abdominal cramps and diarrhoea, while inappropriate relaxation of uterine smooth muscle can result in failed labour.

Effects on smooth muscle are just as likely to curtail a compound's development as effects on heart function, says Crankshaw, who was speaking at a meeting in Boston, MA, USA on *Human Tissues for Drug Discovery through Preclinical Research*, organized by IBC Life Sciences (17–18 November 2003; <http://www.lifesciencesinfo.com/tissues>). 'The potential for developmental compounds to interact with smooth muscles should be taken very seriously,' he said. Smooth muscle is complex, he adds, comprising smooth muscle cells, intrinsic and extrinsic nerves, blood



vessels, and endothelial, endometrial and mucosal layers involved in paracrine interactions.

In silico screening alone is not sufficient for drug development, says Crankshaw, because potential targets remain unknown, even though the list of known targets already spans numerous ion channels, receptors and enzymes.

Therapeutic programs

Drug company Pharmagene in Royston, UK (<http://www.pharmagene.com>) has already demonstrated progress in therapeutic programs initiated from work on human tissues. Human synthetic secretin (PGN0052) has

proven safe and well tolerated in three Phase I studies, improving lung function in normal volunteers and mild asthmatics, the company reports.

A Phase II proof-of-concept study of intravenous PGN0052 in cystic fibrosis patients is 'due to start imminently,' Robert Coleman, Chief Scientific Officer of Pharmagene, told *BioMedNet News* (<http://news.bmn.com>).

Several important considerations face researchers interested in working with human tissue, including the identification of partner organizations, such as hospitals, the ethical and safety issues of using human tissue, and the selection of the best specimens. There are many sources of smooth muscle, including umbilical vessels and tissue removed during lung and colon resection, hysterectomy and coronary bypass surgery.

Although work on human tissue shows promise, animal tissue should not be forgotten. 'It is certainly not my intention to suggest that animals have no place in this process,' said Coleman, 'simply to make their use more informed and efficient.'

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