

## Resolution: Fighting fibrosis with macrophages

BY LAUREN MARTZ, SENIOR EDITOR

Macrophages are emerging as one of the hottest tools in the fight against cancer, but Resolution is targeting a new application for the cells: attacking fibrosis.

The Syncona-backed company launched in August with £26.6 million to develop macrophage cell therapies after the VC and the University of Edinburgh Center for Regenerative Medicine concluded a two-year research collaboration assessing the commercial viability of the technology.

Resolution Therapeutics Ltd. was formed around clinical and preclinical research from co-founders Stuart Forbes of the University of Edinburgh and John Campbell of the Scottish National Blood Transfusion Service (SNBTS) showing the regenerative potential of macrophages in the liver.

“There is a huge body of science understanding the role of macrophages in general. One role is to provide an inflammatory response to injury and infection, and the other is to orchestrate the process of wound healing when the threat of injury or infection has passed,” said Resolution Chairman and CEO Edward Hodgkin. “We’re exploiting the second aspect here.”

He told BioCentury that Forbes’ work demonstrated wound healing macrophages — or M2 macrophages — play key roles in liver repair by breaking down fibrosis, secreting metalloproteases and engulfing or phagocytosing necrotic hepatocytes.

They also stimulate new hepatocytes from progenitors and signal to the immune system to come to the site of injury to assist in wound healing, he said.

“Stuart hypothesized that if we give macrophages of the wound healing phenotype to a scarred liver in fibrosis, we could create an environment whereby the liver would start to regenerate naturally,” Hodgkin added.

Hodgkin said Forbes and Campbell tested their hypothesis in the Phase I, investigator-led MATCH study, where they found “strong evidence of safety and efficacy of non-engineered, autologous macrophages” in nine cirrhosis patients treated in the dose escalation study. They’re now running a Phase II study of the non-engineered macrophages.

### COMPANY PROFILE RESOLUTION THERAPEUTICS LTD.

London, U.K.

**Technology:** Macrophage cell therapy to promote wound healing

**Origin of technology:** University of Edinburgh

**Disease focus:** Hepatic

**Clinical status:** Preclinical

**Founded:** 2020 by John Campbell, Stuart Forbes

**Academic collaborators:** University of Edinburgh

**Corporate partners:** None

**Number of employees:** 16

**Funds raised:** £26.6 million (\$36.3 million)

**Investors:** Syncona

**CEO:** Edward Hodgkin

**Patents:** None issued

Resolution was created to build on the academic work with engineered versions of the cell therapy.

Hodgkin provided few details about how the cells would be engineered, but told BioCentury the company is testing whether it’s necessary to lock the cells into the wound healing phenotype.

Resolution will initially develop autologous cell therapies, which are created when circulating monocytes are extracted from a patient using leukopheresis, then differentiated into macrophages and engineered ex vivo before they’re returned to the patient intravenously.

Hodgkin said the liver makes a good initial target because intravenously delivered cells naturally home to the organ. The company’s initial indication is compensated cirrhosis, but it will also assess whether the cells have potential in other fibrotic diseases such as pulmonary fibrosis and chronic kidney disease.

Hodgkin said targeting cirrhosis allows the company to test the cells in patients from diverse etiologies including non-alcoholic steatohepatitis (NASH), alcoholic cirrhosis and viral hepatitis. “I think Hepatitis C virus patients who’ve been cured of the

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infection but have persistent fibrosis are a particularly interesting group because the etiology has been removed,” he said.

The £26.6 million series A round gives Resolution about four years of runway, during which time the company plans to build the platform, establish manufacturing and bring engineered cells into a clinical trial for compensated cirrhosis.

“There are no companies doing macrophage cell therapies. We have to build the infrastructure, and we have to build it all the way ourselves if we want a sustainable business,” Hodgkin told BioCentury.

Resolution has a collaboration with SNBTS, which provided clinical macrophage material for the MATCH academic trial. “Our process is going to adapt that and add in engineering steps, but it’s a good starting point for our manufacturing process,” he said.

Syncona has a history of launching and investing in cell and gene therapy companies, with a strategy focused on de-risking the technology by investing in scalable and sustainable manufacturing. Its portfolio includes neoantigen T cell companies Achilles Therapeutics Ltd. and Neogene Therapeutics Inc., regulatory T cell company Quell Therapeutics Ltd., and TCR/CAR T cell company Autolus Therapeutics plc (NASDAQ:AUTL).

In the future, Resolution might also explore off-the-shelf macrophage therapies, and possibly related partnerships. “This would be very attractive, but there are technical challenges with the repeat dosing we think will be required for macrophages and the immunogenicity risk, and those would have to be overcome,” Hodgkin said.

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