

CRT Opportunity



Senectus Therapeutics Limited

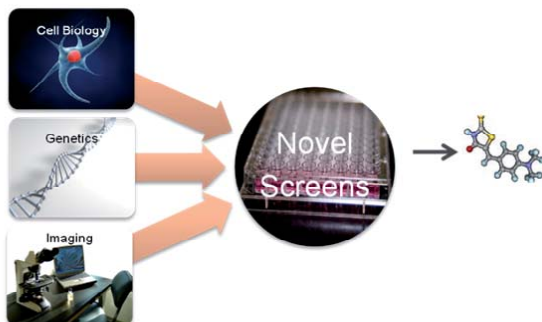
- New drug discovery company focused on cellular senescence.
- Targeting senescence offers the potential for future cancer therapies complementary to existing interventions aimed at apoptosis
- Founded around a unique, custom built, multi-disciplinary consortium of cutting-edge UK scientists
- Part of a CRT initiative which, in collaboration with Cancer Research UK, is seeking to tackle some of cancer's most intractable scientific challenges
- Senectus has secured \$1M in translational funding and is seeking collaboration or investment

SMALL MOLECULES | Assay Development & Early Screening

September 2009

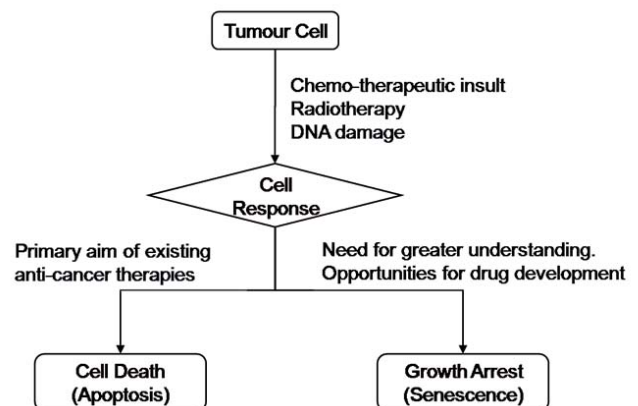
The Concept

Senectus Therapeutics Ltd is a new venture for CRT. It is founded on a hand-picked consortium of key UK scientists whose research expertise in telomere biology, autophagy and tumour suppression is being utilised to develop innovative drug screening techniques. In conceiving Senectus, the primary objective was to bring together world leading CRUK expertise in mammalian cellular senescence along with new and advanced technologies in cell engineering and imaging to generate a toolbox of high content screening techniques, reagents and tools. Ultimately, the outcome of the initiative will be identification of critical paths for cellular senescence, development of screens for compounds modulating senescence and small molecules and target leads for drug development and pathway manipulation.



Therapeutic Rationale

Cellular senescence is an irreversible arrest of cell proliferation. One of the fundamental changes that underpins cancer is escape from apoptosis and/or cellular senescence. Whereas apoptosis is a key target pathway of current anti-cancer therapies, senescence is a comparatively unmined target pathway. The senescence pathway therefore offers potential targets for new cancer therapies complementary to existing interventions aimed at apoptosis.



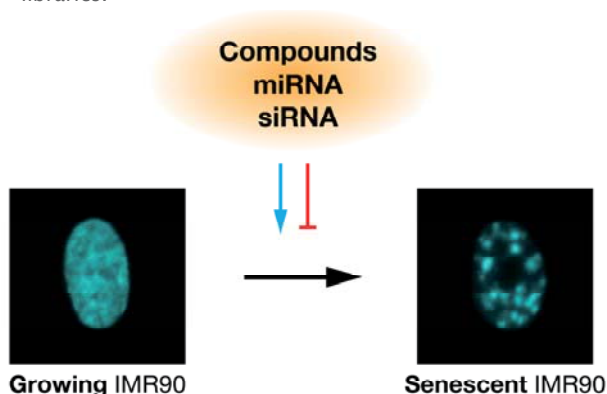
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The Senectus Team

Professor W Nicol Keith CRUK Beatson Laboratories University of Glasgow	Expertise in cell senescence/immortality & cell-based screening.
Dr Masashi Narita CRUK Cambridge Research Institute University of Cambridge	Expertise in cell senescence and chromatin biology
Professor Dorothy Bennett St George's University of London	Expertise in melanoma biology and cell senescence
Professor Mike White University of Liverpool	Expertise in single cell imaging
Dr Chris Torrance Horizon Discoveries Ltd	Expertise in cell engineering, drug discovery and development
Cancer Research UK/Cancer Research Technology Ltd	Expertise in drug discovery and development and project management

Progress to date

- Proprietary cell-based screens established for key signalling pathways regulating and maintaining senescence.
- Advanced imaging technologies developed to support high-content screening.
- Novel isogenic human cell lines engineered to express senescence-associated genes are being utilised within high-content screens.
- Proof-of-concept screening completed with small-molecule libraries.



Intellectual property

Intellectual property arising from the research is owned by Senectus. Patents will be filed on small molecule series as they emerge.

Commercial opportunity

CRT is seeking a partner to enter in to an investment and/or co-development arrangement with Senectus.

References

Keith, W.N. *et al.* Seeding drug discovery: integrating telomerase cancer biology and cellular senescence to uncover new therapeutic opportunities in targeting cancer stem cells. *Drug Discov. Today*. 2007;12(15-16):611-21.

Atkinson S.P. & Keith W.N. Epigenetic control of cellular senescence in disease: opportunities for therapeutic intervention. *Expert Rev. Mol. Med.* 2007; 9(7):1-26.

Chiantore M.V. *et al.* Senescence and cell death pathways and their role in cancer therapeutic outcome. *Curr. Med. Chem.* 2009;16(3):287-300.

Prieur A & Peeper D.S. Cellular senescence *in vivo*: a barrier to tumorigenesis. *Curr. Opin. Cell Biol.* 2008;20(2):150-5.

CRT

CRT is an oncology focused development and commercialisation company. Senectus Therapeutics receives project management and commercial support from CRT. It is one of a robust pipeline of commercial opportunities currently available from CRT.

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