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IDEAS TO LIFE RANGAHAUA KIA WHAI HUA

Tumour Targeted Irreversible FGFR inhibitors

A targeted approach to deliver potent irreversible FGFR inhibitors utilising hypoxia selective activation for cancer therapy.

Background

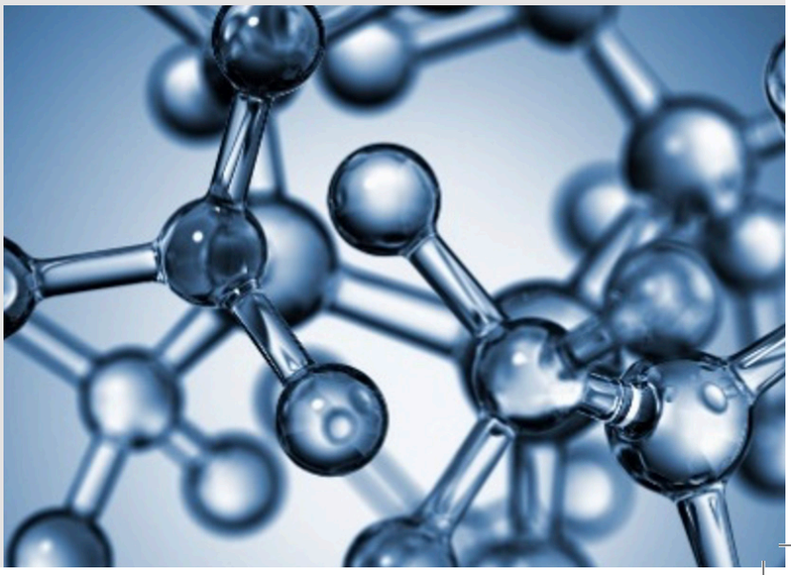
The human fibroblast growth factor receptor (FGFR) family are a subfamily of receptor tyrosine kinases (FGFR1, FGFR2, FGFR3, FGFR4) that facilitate FGF binding and activate multiple cellular signalling cascades. FGFRs regulate important biological processes including cell growth, proliferation, differentiation and survival. Numerous human pathological conditions are associated with FGFR signal deregulation, including a variety of cancer types through FGFR gene amplifications, fusions or activating mutations.

Hypoxia-activated FGFR TKIs

Extensive knowledge on tumour hypoxia and kinase inhibitor chemistry has resulted in the development of a novel series of potent, irreversible FGFR1-3 inhibitors currently at lead stage. A bioreductive trigger has been identified that permits targeted release of FGFR inhibitors in the hypoxic tumour environment. The resulting prodrugs allow targeted control of FGFR gain-of-function anomalies, for therapeutic benefit at higher efficacy and with fewer off-target systemic effects. The lead inhibitor and prodrugs are patent protected in the US, China, and New Zealand, with additional territories in progress.

Major advantages

- Exploits hypoxic tumour environment – targeted release without the requirement to distinguish between native and cancer-driving FGFR.
- Improved therapeutic window – prodrug technology results in less risk of off-target and on-mechanism toxicity, allowing more effective treatment scheduling than leading clinical FGFR inhibitors.
- Established technology – the bioreductive trigger that controls hypoxia-selective release has previously been evaluated in clinical trial.
- Predictive biomarkers – the major contributing enzyme for inhibitor release (STEAP4) has been identified, allowing improved patient selection and response rates.



Applications

- Targeting FGFR activity has the potential to treat various cancer types where FGFR1-3 are upregulated, such as:
  - Urothelial
  - Breast (triple negative)
  - Endometrial
  - Esophageal
  - Gastric
  - NSCLC
  - Ovarian
  - Prostate
  - Multiple myeloma

UniServices by the numbers

Total external research funding:
$261.3M
(35% increase over 2020)

45
companies started in the past five years

$1.25BN
Total market capitalisation of companies formed

$73.5M
Net asset value of the University of Auckland Inventors' Fund

17,335 Covid-19 vaccinators trained by the Immunisation Advisory Centre in 2021

1,700
New Zealand teachers reskilled and upskilled through Tui Tuia | Learning Circle professional learning and development in 2021

3,000
clinical staff at 22 DHBs trained through teamwork-based acute care simulations designed by NetworkZ in the past five years

14,391 times that child and youth mental health workers attended Whāraurau e-modules, trainings and workshops in 2021

UniServices

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University of Auckland

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