Open Briefing 6 December 2017

NOXOPHARM

ONCOLOGY

NOX66 Idronoxil (lipophilic form)

ABOUT IDRONOXIL

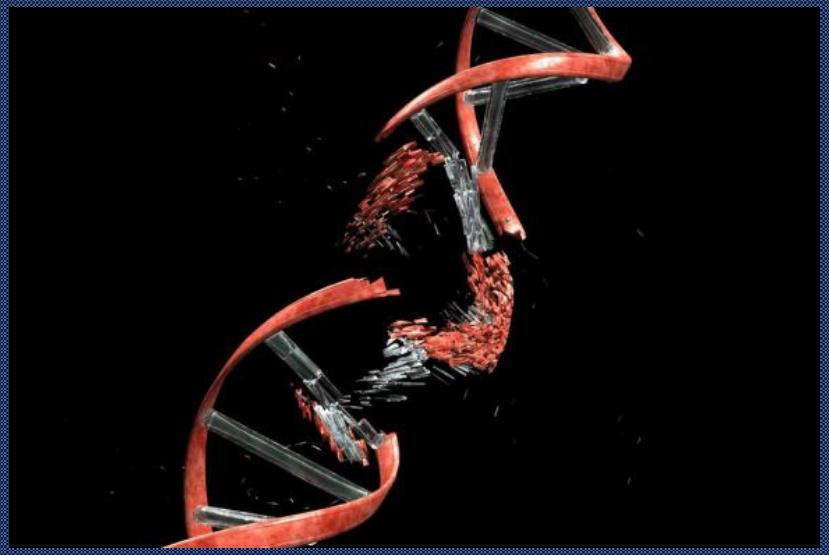
Multiple anti-cancer actions

1. Inhibits DNA repair

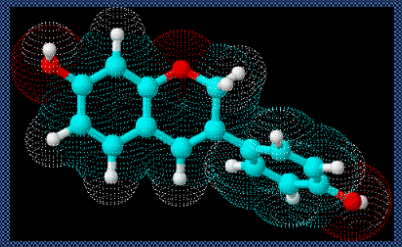
(inhibits PARP-1, topoisomerases 1 and 2)

2. Promotes anti-tumour immunity

(Increases NK (natural killer) cell activity)



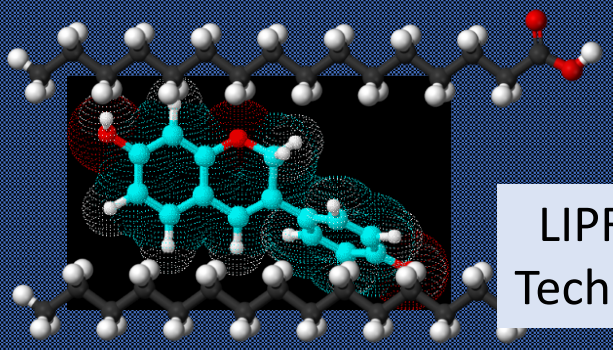
Oral Idronoxil



Excreted quickly (45 min)

Does NOT cross BBB

NOX66



LIPROSE Technology

Excreted slowly (10 hours)

Crosses BBB

Noxopharm

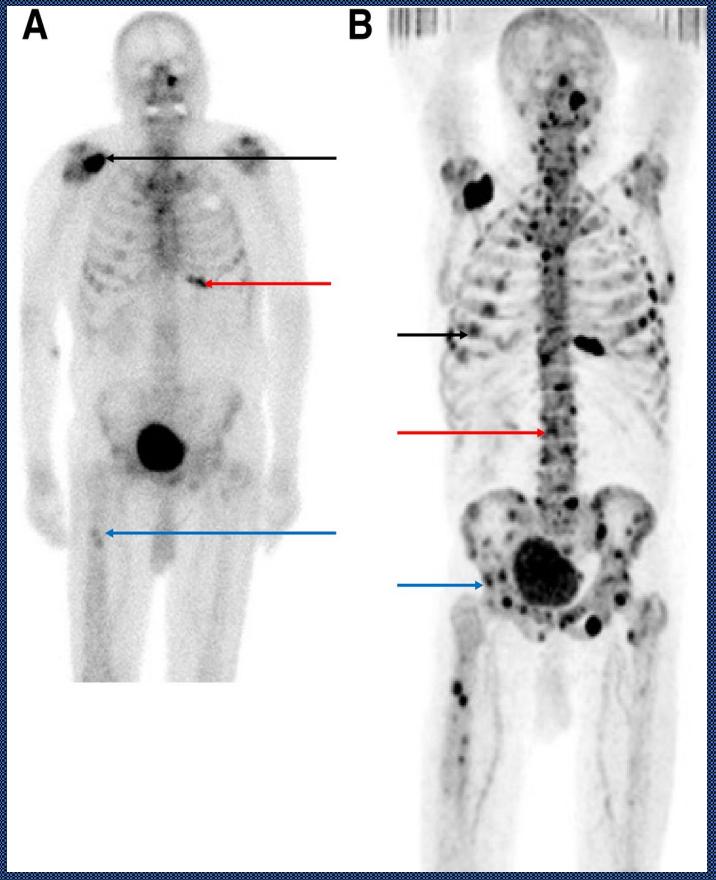
DARRT

Direct and Abscopal Response to Radio-Therapy

Limitation of radiotherapy

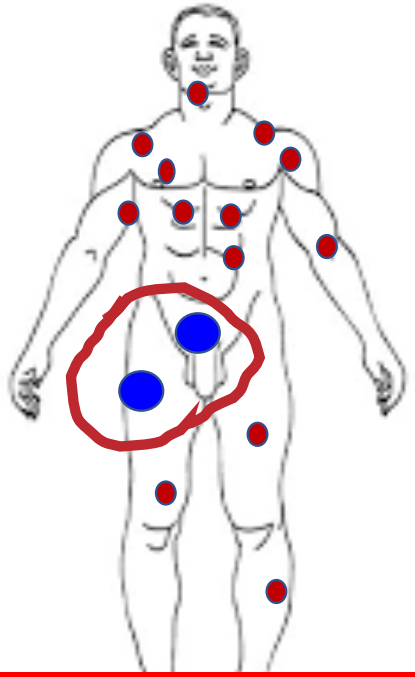
Metastatic cancer too extensive for radiation

Noxopharm

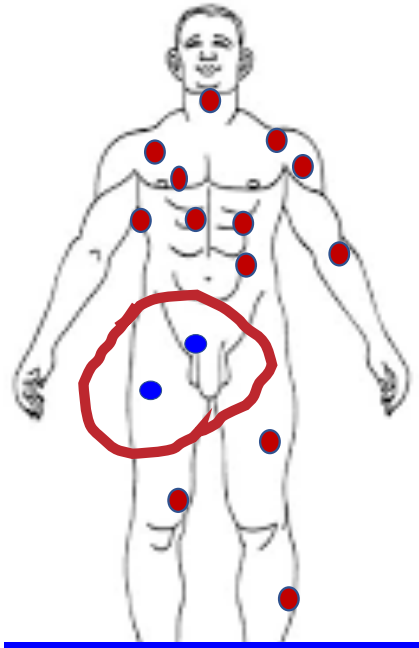


DIRECT Response to Radio-Therapy

Noxopharm



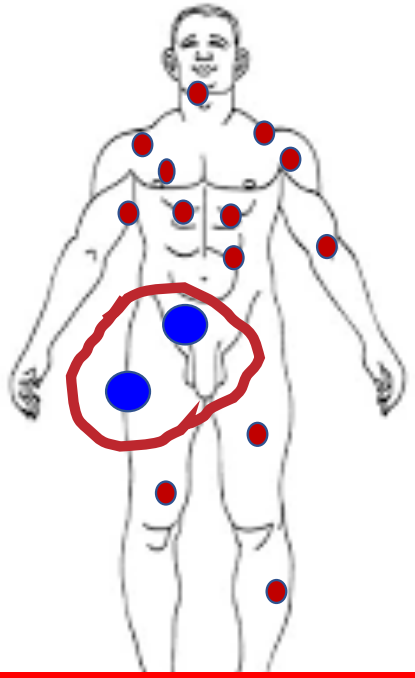
Radiotherapy applied to large tumours for pain relief



Shrinkage of irradiated tumours

DIRECT Response to Radio-Therapy

Noxopharm



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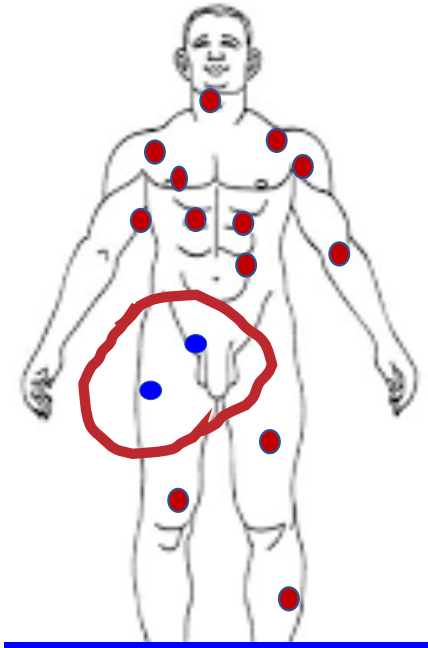
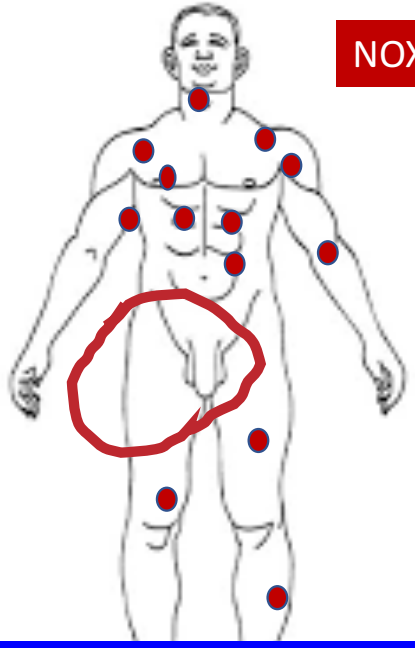


Shrinkage of irradiated tumours



NOX66

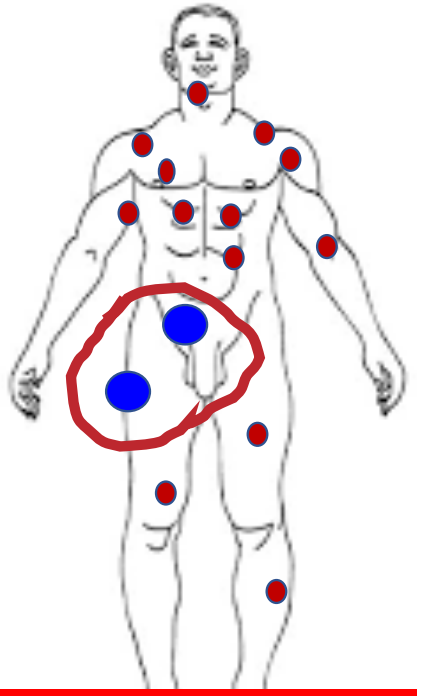
Seeking complete remission of irradiated tumours

ABSCOPAL Response to Radio-Therapy

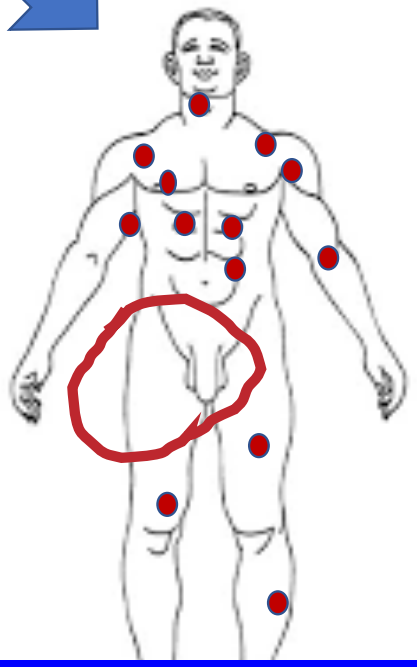
Noxopharm

Exposed tumours respond

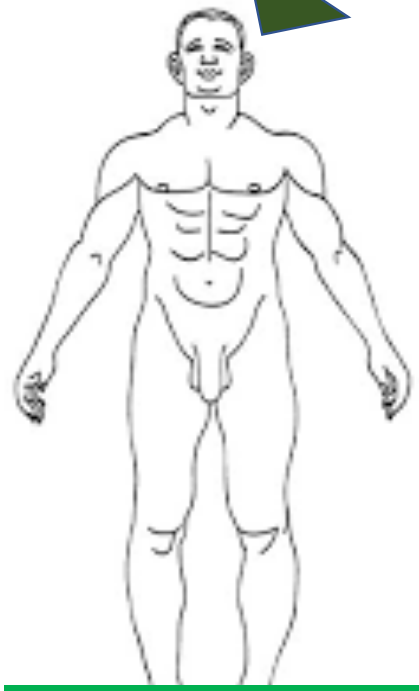
✚ Non-exposed tumours also respond



Low-dose radiotherapy



Seeking **complete remission** of irradiated tumours



Abscopal response

Features of an abscopal response

Rare – very rare phenomenon
Complete – primary AND secondary tumours respond
Durable – potentially permanent
Unrestricted – range of cancers reportedly involved
Short treatment – single course of treatment (7-14 days)
Low toxicity – low-grade radiation sickness

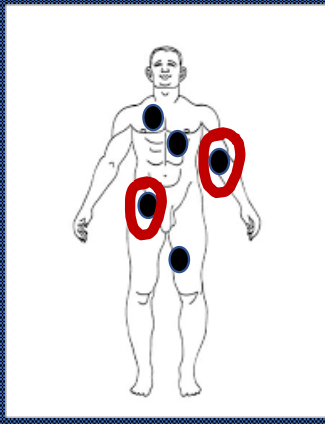
DARRT

Direct Effect

Abscopal Effect

External Beam RT

- Patients with multiple (>3) tumours
- Irradiate 1-2 tumours (5 days)
- NOX66 14 days
- Scan + 2 months and 4 months



DARRT

Direct Effect

Abscopal Effect

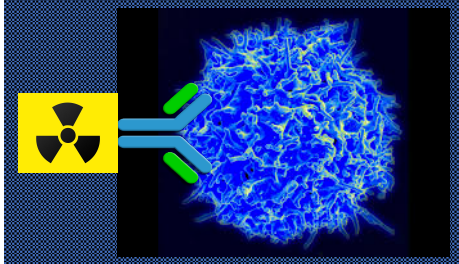
External Beam RT

- Prostate cancer (metastatic castrate-resistant)
- Solid common cancers (eg. lung, breast, melanoma)
- Rare cancers (eg. sarcomas)

DARRT

Direct Effect

Abscopal Effect



Brachytherapy

- ^{177} Lutetium-PSMA-617
- 4 x monthly intravenous injections of LuPSMA/10 days NOX66
- Prostate cancer (metastatic castrate-resistant)

DARRT

Where NOX66 + Radiotherapy needs a boost ……

NOX66-001 Phase 1b Study Georgia

+ Low-dose carboplatin (AUC4 – monthly)

400 mg NOX66	5 patients: 1 progressive; 4 non-progressive
800 mg NOX66	7 patients: 1 progressive; 5 non-progressive; 1 partial response

What will a 'good response' look like ?

- Lung Cancer trial (**582 patients** evaluated)
- Opdivo vs standard chemotherapy
  - Survival of 50% of patients - **12.2 months v 9.4 months**
  - Time to disease progression – **2.3 months v 4.2 months**
  - Overall Response Rate – **19% v 12%**
    - Four Complete Responses v One
  - Adverse Reactions **(>20% of patients**) - fatigue, musculoskeletal pain, cough, breathing difficulty, decreased appetite

- US$150,000 treatment cost
- Sales for first 6 months 2016 = US$1.6 billion

http://www.opdivohcp.com/metastatic-nsclc/efficacy/clinical-trial-results

Noxopharm

Moving towards first registration

Target Indication: NOX66 in combination with Radiotherapy for the treatment of patients with metastatic cancer

Studies:

- NOX66-002A: Determine Dose of NOX66 (Prostate Cancer)
- NOX66-006: Open Label, all tumours. Safety and efficacy
- NOX66-007: Randomised, 2-3 tumours. Efficacy in comparison to standard care
- LuPIN Study: ^{177}Lu-PSMA and NOX66 (Prostate Cancer): Supporting registration
- Expansion of ^{177}Lu-PSMA research
- Other Radiotherapy Research (supportive data, for expanded indication in future) – e.g. brain, paediatrics, stereotactic, brachytherapy etc.

Submit for Registration

2017 | 2018 | 2019 | 2020/21

Notes:

- Different Global Regulators may modify indication for specific tumour types
- Indication may also list when treatment can be used
- Indication will discuss how to use Radiotherapy with NOX66
- Rare cancers may not be included in indication, however evidence is important
- Reimbursement is as important as Registration

Beyond the trials to reach registration

- **Manufacturing and formulation:** Optimise NOX66 formulation; GMP Manufacturing
- **Pre-clinical / non-clinical**: *in vitro* and animal studies to meet regulatory and other requirements for registration and marketing

NEW!!

- **Medical Affairs:** Liaison with oncologists, advisory boards, congress attendance and presentation

NEW!!

- **Marketing:** Develop Noxopharm presence, brand-naming, commercialization (including pricing) strategy

Communicating Trials Progress 2018

- Progress – based on Data Safety Monitoring Committee Review
  - Independent body – researchers and statisticians
  - Regular meetings during trials – expect ~6 across trials in 2018
  - Review overall progress → decisions on continuation
  - Findings of DSMBs will be communicated

- Trial Data at conferences
  - Contingent on significant milestones in trials (end of study, all patients through a pre-defined time point) – expect ~4 in 2018
  - Requires considerable planning (e.g. ASCO – meeting June, submit presentation in February)
  - Requirement that data are embargoed until presented
  - Where significant outcomes, top line result may be released as per ASX requirements prior to conference


Nyrada
inc

Nyrada inc

2 technologies

- LIPROSE
- P-PDT

3 drugs

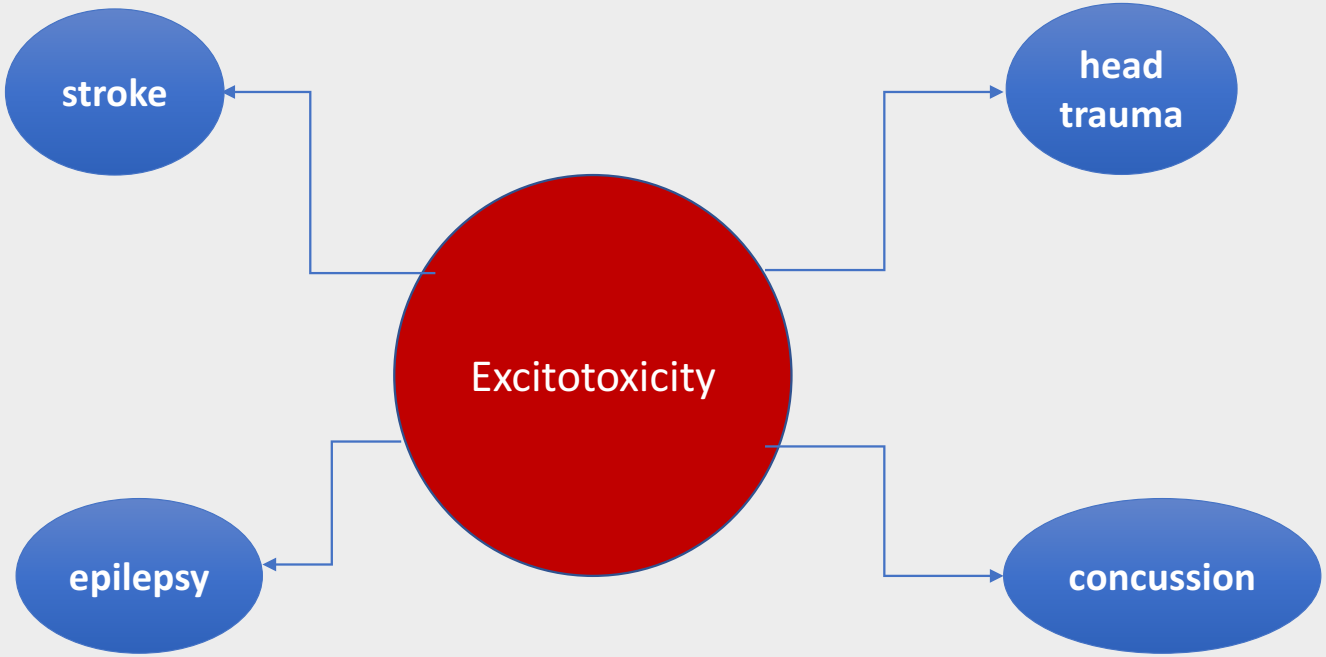
3 indications

- Stroke
- Concussion
- Severe epilepsy

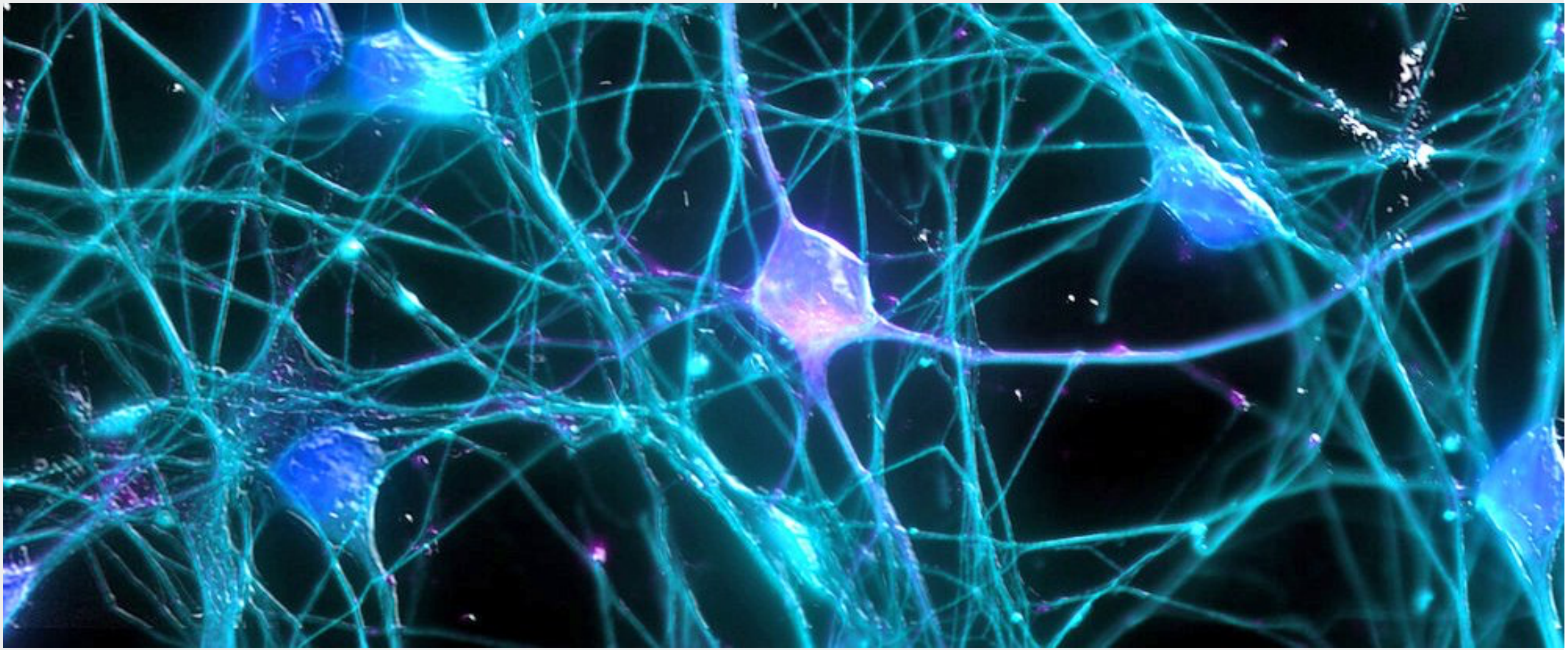
Peripheral neuropathy

Hypercholesterolaemia

NYX-104 Inhibitor of *excitotoxicity*

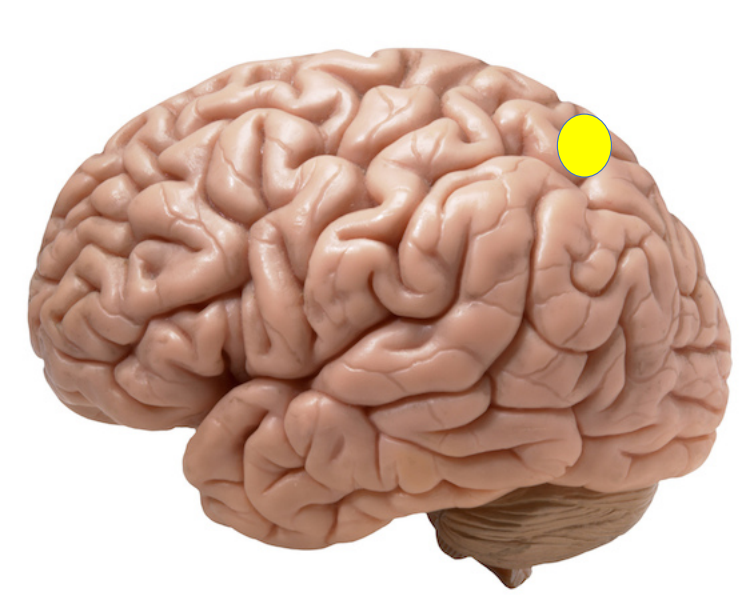


NYX-104

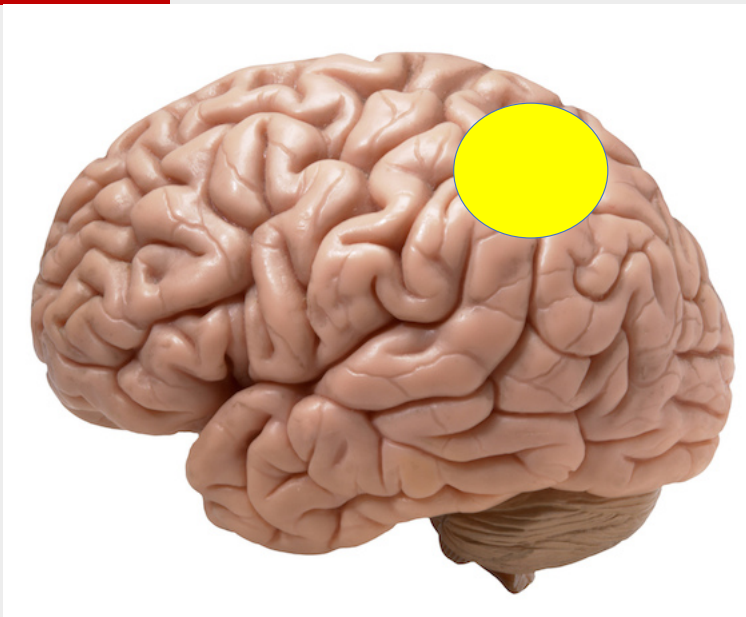


NYX-104

Excitotoxicity



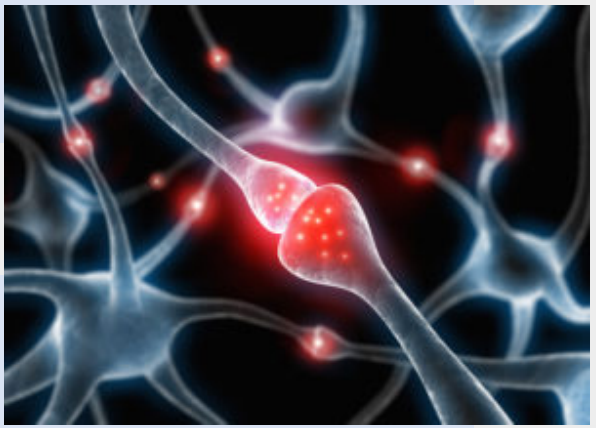
Size of original area of damage from stroke or concussion



Days to weeks later, excitotoxicity has increased area of damage up to **10-times**

NYX-104

1. University of NSW Translational Neuroscience Facility:
   Breakthrough identification of key protein promoting excitotoxicity (**TrpC3 isotope**)

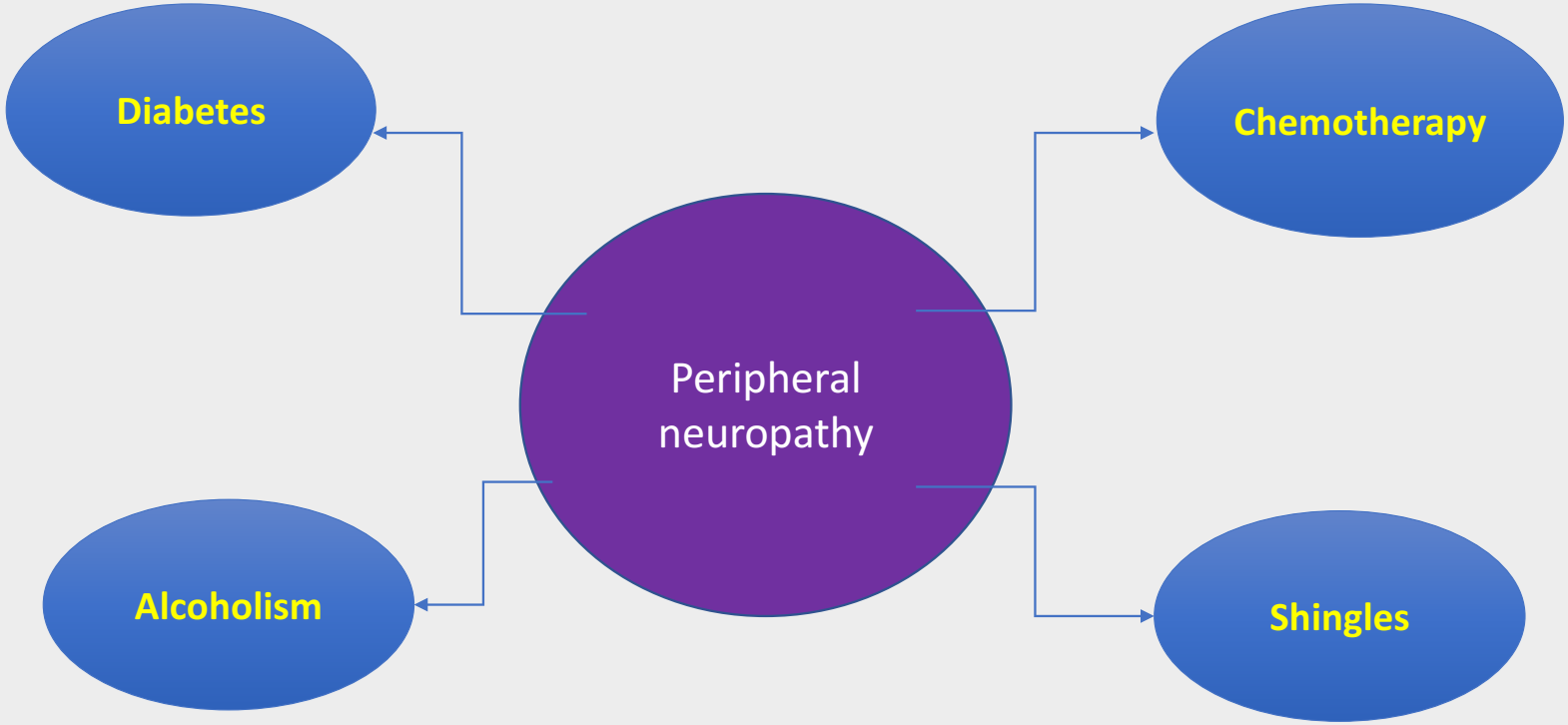


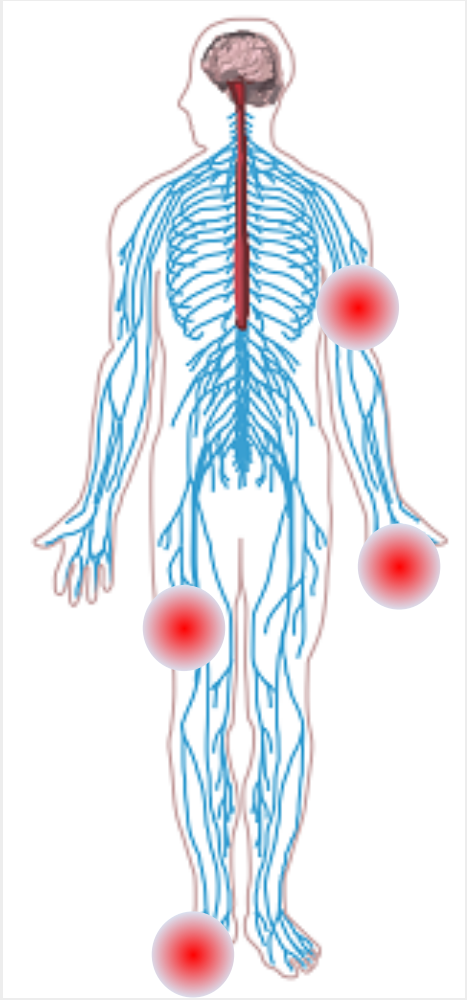
2. *In vitro* screen of NOX compounds:
   NYX-104 inhibits TrpC3

3. Mouse model of human stroke:
   NYX-104 is potent inhibitor of excitotoxicity.
   70% reduction in area of brain death post-stroke.

NYX-205

Anti-inflammatory
Designed to cross the blood-nerve barrier





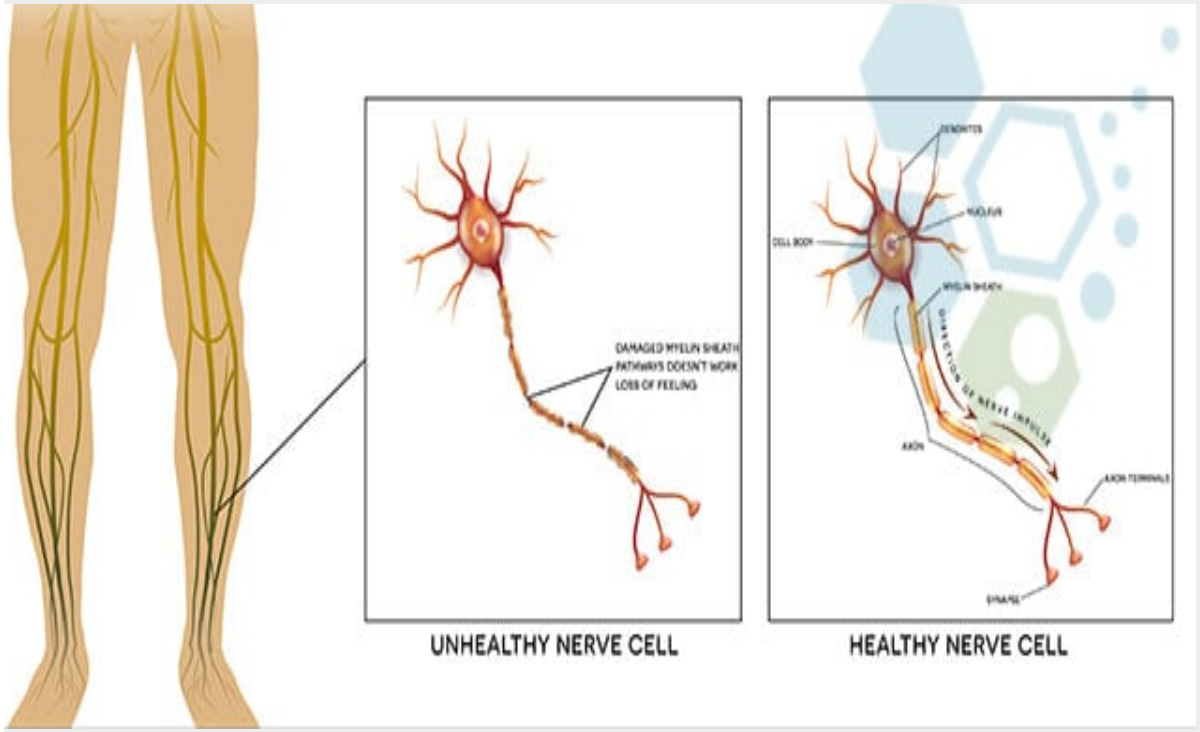
NYX-205

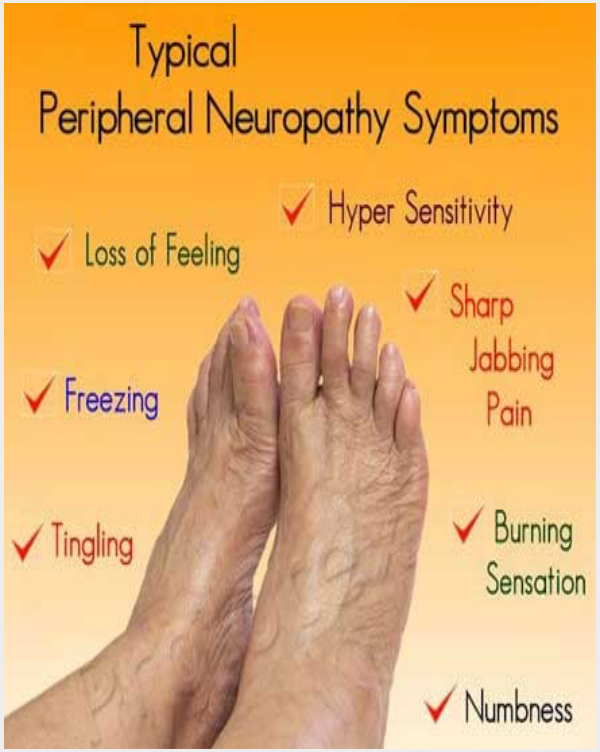
Peripheral neuropathy

Incidence in US estimated at 20 million:

- Diabetes
- Alcohol abuse
- Chemotherapy

Blood-nerve barrier is major obstacle to effective treatment. NYX-205 designed to cross this barrier.





NYX-205

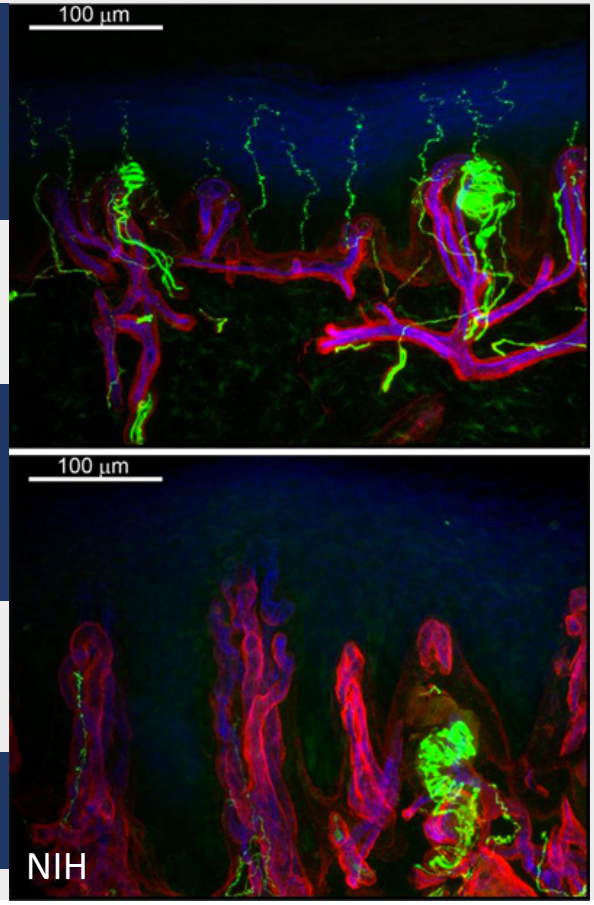
Peripheral neuropathy

Nyrada inc

Targeting peripheral neuropathy in cancer patients receiving chemotherapy

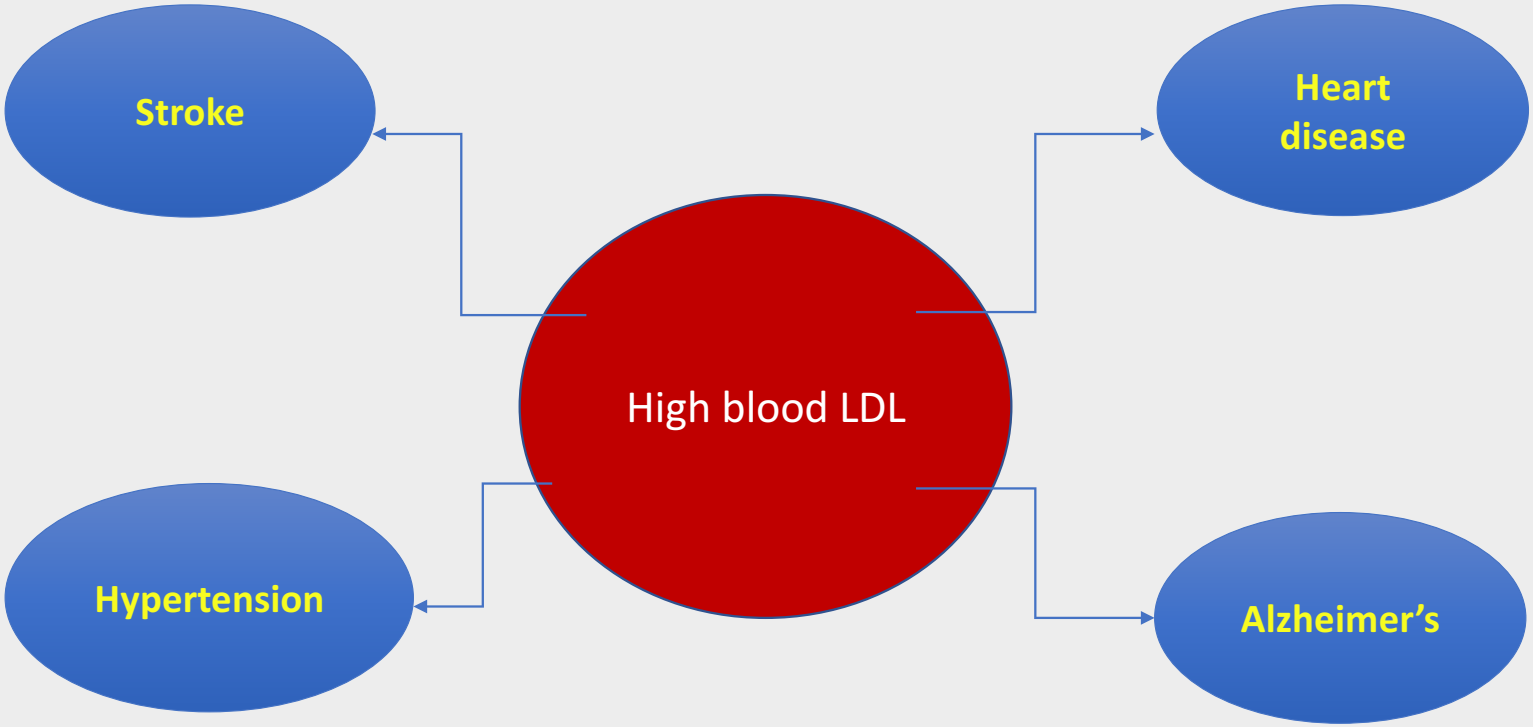
60% incidence at 3 months
30% incidence at 6 months

Currently no effective treatment



NYX-330

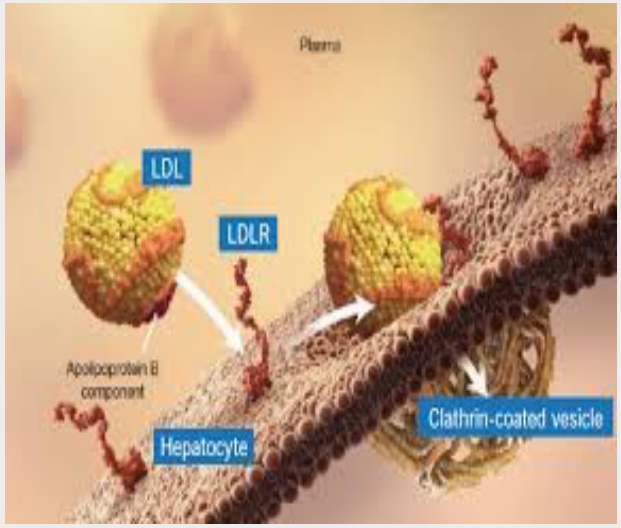
Hypercholesterolemia



NYX-330

Hypercholesterolemia

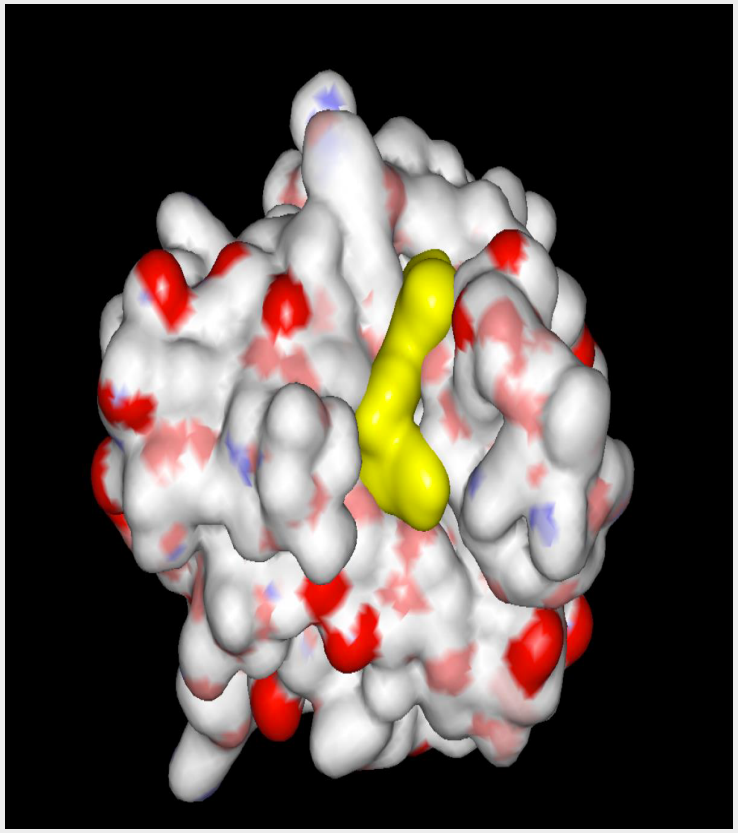
- **PCSK9** identified as superior drug target compared to statin drugs for lowering blood LDL levels.
- **PCSK9** is plasma protein that binds to the LDL-LDL receptor complex, preventing recycling of the LDL receptor and thereby increasing LDL levels.



PCSK9 declared an unsuitable target for small molecule drug. Amgen develops monoclonal antibody. ***Repatha*** comes to market in 2015.

NYX-330

Hypercholesterolemia



Suitable binding site identified on **PCSK9** for attachment of small molecule.

NYX-330 blocks binding of PCSK9 to LDL- LDL receptor complex.

Nyrada inc

- US-registered
- Focus on small molecules, non-oncology
- 67% owned by NOX; 33% Altnia Holdings
- Currently public unlisted; proposed US listing in 12-18 months

Nyrada inc

OFFER:

- Raise = AUD$6,000,000
- Seed capital = 1,500,000 New Shares
  (A$4 each; 2 Options per 3 Shares)
- Capital structure post-exercise of Options
  - NOX 50%
  - Altnia 25%
  - Seed investors 25%

Application for Shares by sophisticated investors, non-US residents only.
Information Memorandum available: info@nyrada.com

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