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Chronic pain – a high unmet medical need

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Humanity has experienced pain through history …

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Definition: Pain is an unpleasant sensory and emotional experience

- One out of five individuals worldwide suffer from significant longstanding chronic pain
- 7-8% suffer from neuropathic pain.
- Direct costs equal 0.5-2% of EU GNP costs
- Single most common reason for work disability *(the Work Foundation, OECD)*
- Is associated with higher economic burden, poorer quality of life, worse mental well-being and lower physical functioning
- The chronic pain population is particularly vulnerable – suicide risk as high as in depression.
- The increased risk for suicide is linked to the intensity of pain

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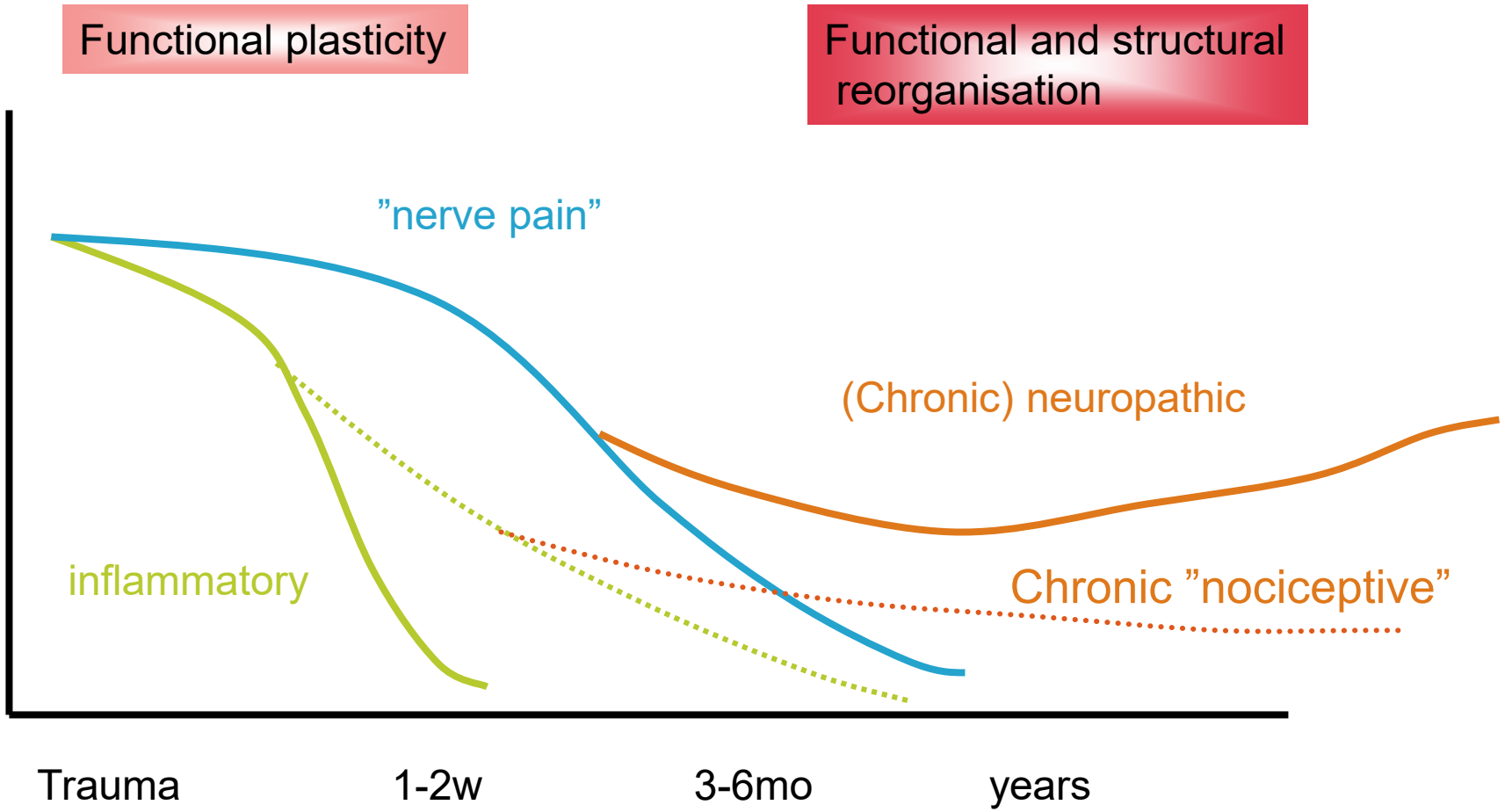
Acute and Chronic pain is not only a question of time



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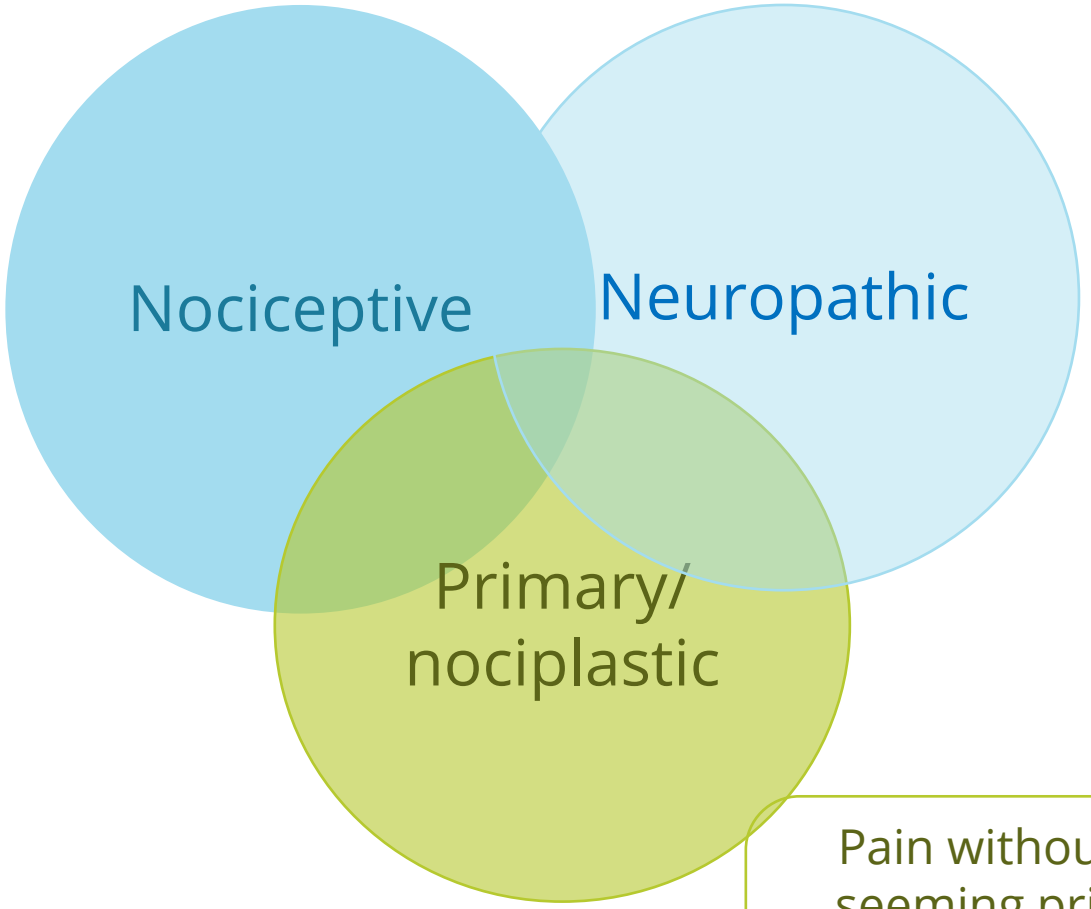
Different types of pain

Pain due to damage to non-neural tissue and is due to the activation of nociceptor:

Osteoarthritis, gout, trauma, tumours, rheumatoid diseases, visceral pain



Pain due to an injury or disease affecting the peripheral or central nervous system, e.g.:

Peripheral neuropathy, chemotherapy induced, post surgical after expected healing

Pain without any seeming primary cause, e.g.:

Fibromyalgia, migraine

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Nociceptive Pain – Typical conditions

- E.g. Osteoarthritis (OA), chronic low back pain, includes both joints and adjacent tissues
- Over 240 million people worldwide suffer OA pain, 12% of adults have chronic low back pain
- Standard of Care NSAIDs have poor efficacy
  - As do second line analgesics: opioids, intra articular steroids
- Treatment gaps
  - 5 out of 6 do not get sufficient pain relief with existing therapies
  - Due to non-response, side effects or high risk for worsening of other common conditions
  - Anti-NGF antibodies not approved based on risk-benefit
- Currently this is substantial research to identify disease mechanisms to then develop disease modifiers, but nothing there yet

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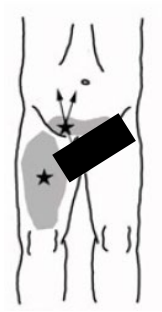
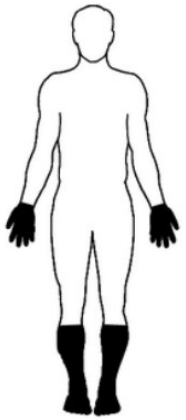
Peripheral Neuropathic Pain

- In the great majority of patients, this is a life-long condition
- The population includes patients with painful diabetic polyneuropathy, chemotherapy induced pain, post nerve injury pain, post herpetic neuralgia, as well as several other backgrounds
- Patients often have an increased pain response than normal or even feel pain on normally not painful stimuli, as well as ongoing pain
- Pain provoking stimuli add substantially to ongoing pain





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Neuropathic pain – Common but "invisible"

- After surgery, 8-10% of patients suffer pain lasting for more than 3-6 months
- One out of five of people with cancer have cancer-related neuropathic pain, as a result of the disease or its treatment
- Worldwide, 47 million individuals suffer from painful diabetic neuropathy, increasing with increasing rate of diabetes
- One out of 4 people will experience shingles, 10% of them will develop chronic postherpetic neuralgia
- Worldwide, 33 million people have HIV, 35% suffer neuropathic pain, unresponsive to treatment

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The impact of chronic pain

- Health-related quality of life for individuals with chronic pain is rated as low as for those with depression, heart disease or poorly controlled diabetes
- Chronic pain also affects family and friends
- Quality of life is more dependent on the severity of the chronic pain than on its underlying cause
- Neuropathic pain is generally more severe, and is associated with worse health, compared to non-neuropathic pain
- Seventeen percent of those who had pain with neuropathic characteristics had health-related quality of life scores equivalent to “worse than death” in a U.K. study

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One tool does not fit all…

… instead we need to have a tool kit enabling us to give the right treatment to the right patient

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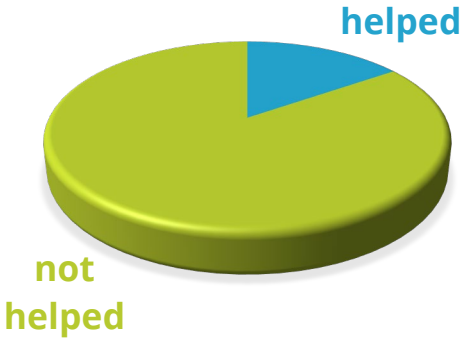
There is a high unmet need in treatment options for neuropathic pain

- The standard of care first line treatments have poor efficacy

DULOXETINE

GABAPENTIN/ LYRICA



LIDOCAINE PATCH

- Other less common treatments, second or third line treatments include capsaicin patches, other antidepressants and antiepileptics, botulinum toxin
- Opioids are third-line treatments
- In all, less than one in three respond in clinical trials, in real life data, it is in the range of one in 7 individuals

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There is a high unmet need also in chronic nociceptive pain

- In acute and chronic low back pain, nonsteroidal anti-inflammatory drugs (NSAIDs), like naproxen, ibuprofen, celecoxib, are used, but they help less than one in 10 or more
- These should also not be taken regularly by people with cardiovascular disease, asthma, gastritis, inflammatory bowel disease, renal failure…
- Topical NSAIDs are good for sprains and strains but have limited efficacy over time
- Opioids are used in severe acute pain, but are also used in chronic pain, without evidence and with troublesome effects

- In summary, available options give limited effect in one of 6-7 patients, and carry troublesome side effects

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The opioid epidemic in the US has put a focus on side effects of strong pain medications highlighting the need for non-opioid approaches.

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Summary

- Disabling chronic pain affects one in five worldwide
- Patients with chronic pain have a very low quality of life
- Chronic nociceptive and neuropathic has a huge impact on employment, family economy, physical function and mental health
- Direct societal cost are very high
- There is a high unmet need for better, more specific and safer treatments

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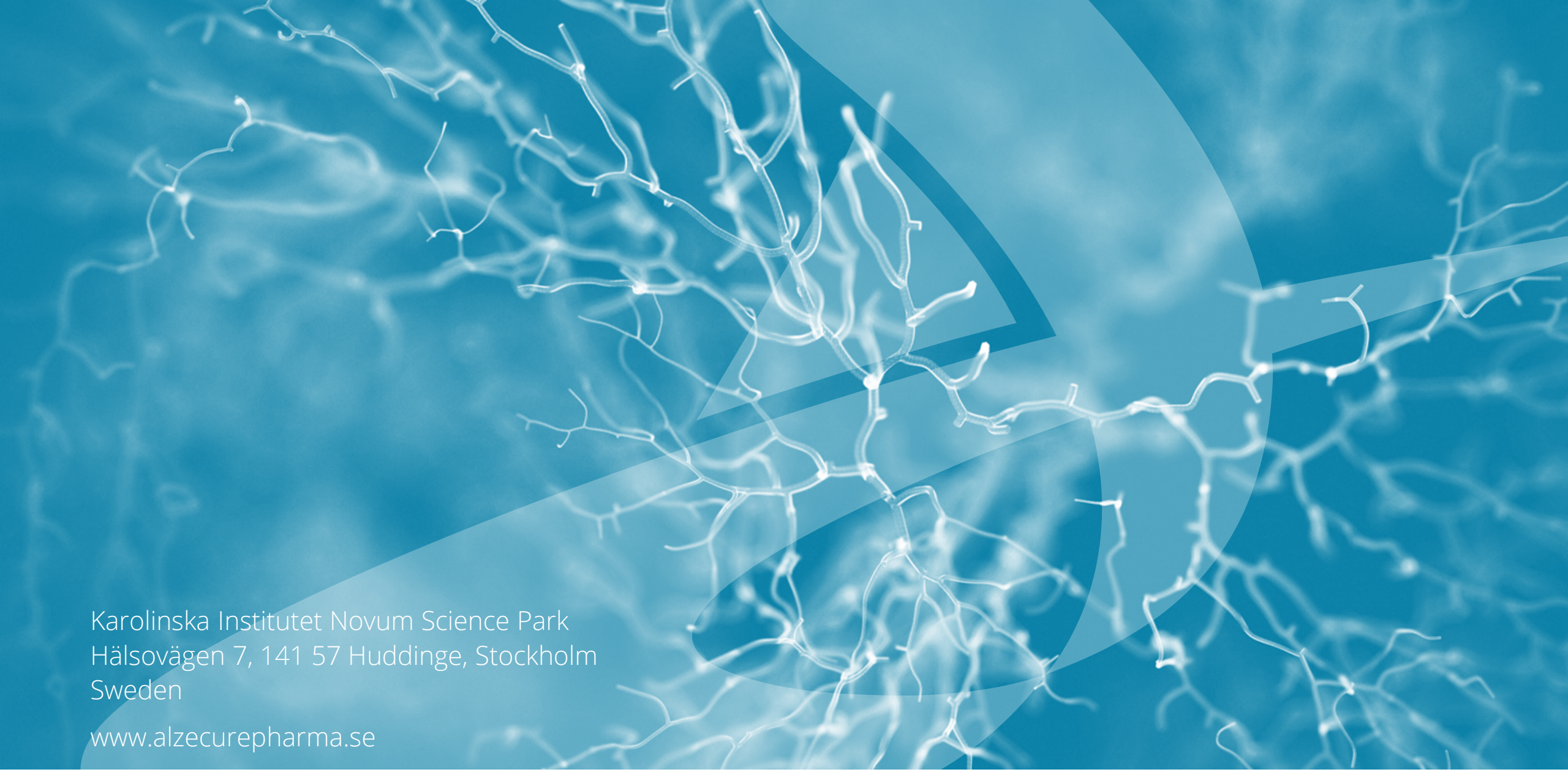

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