

# HNPCC annual meeting

October 12, 2017

Auditorium 1, Hvidovre Hospital

Forsknings- og Undervisningsbygningen

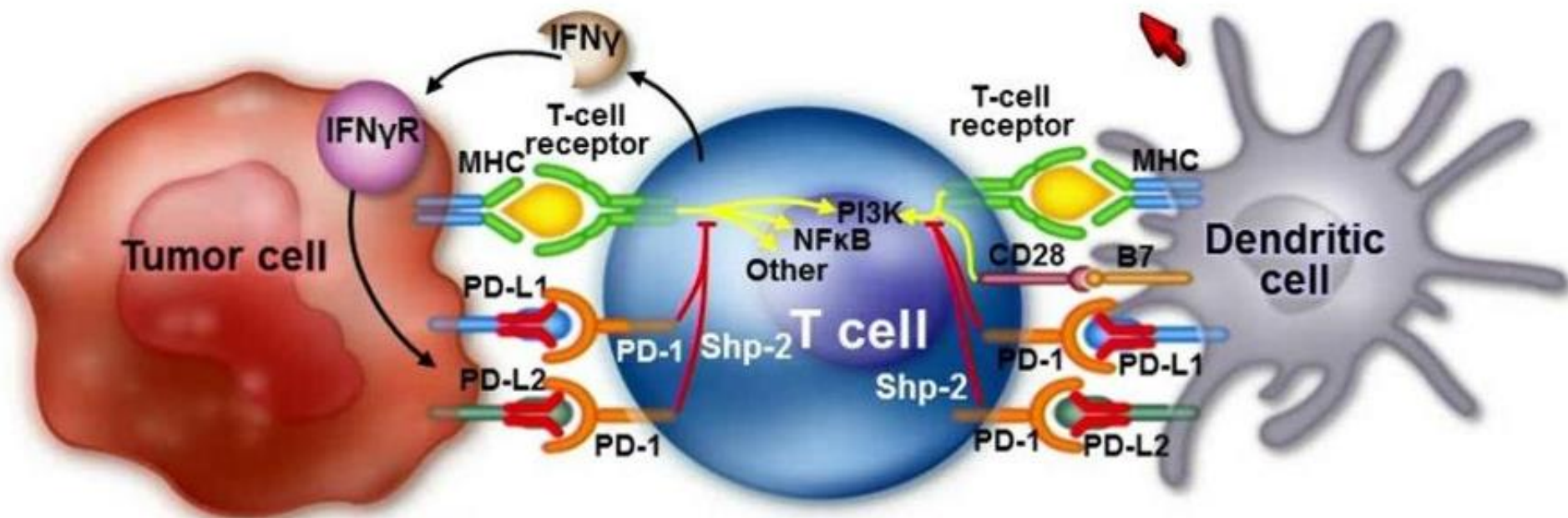


# Immunotherapy in Denmark

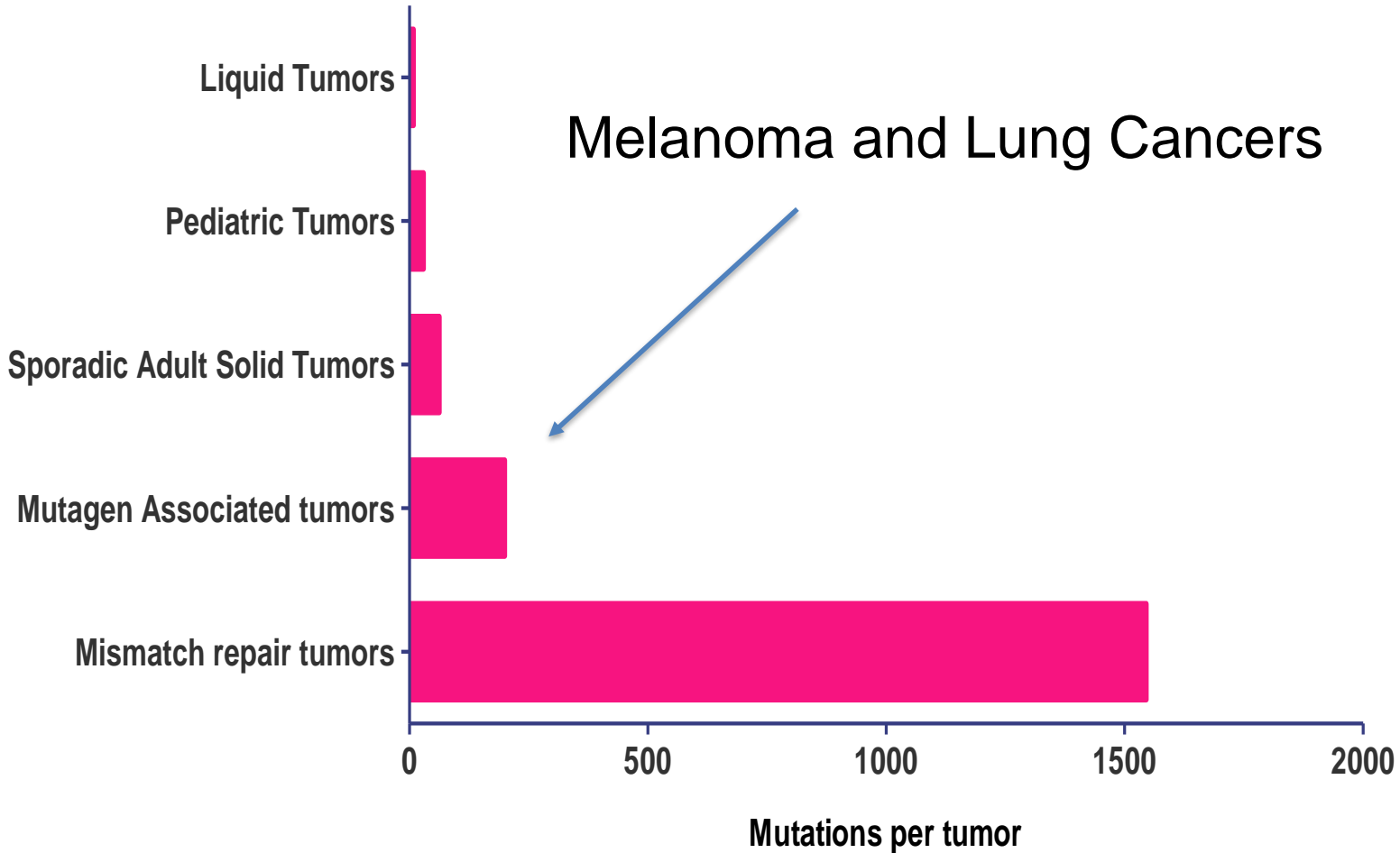
Lars Henrik Jensen, Ph.D., Department of  
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# Immunotherapy in Denmark

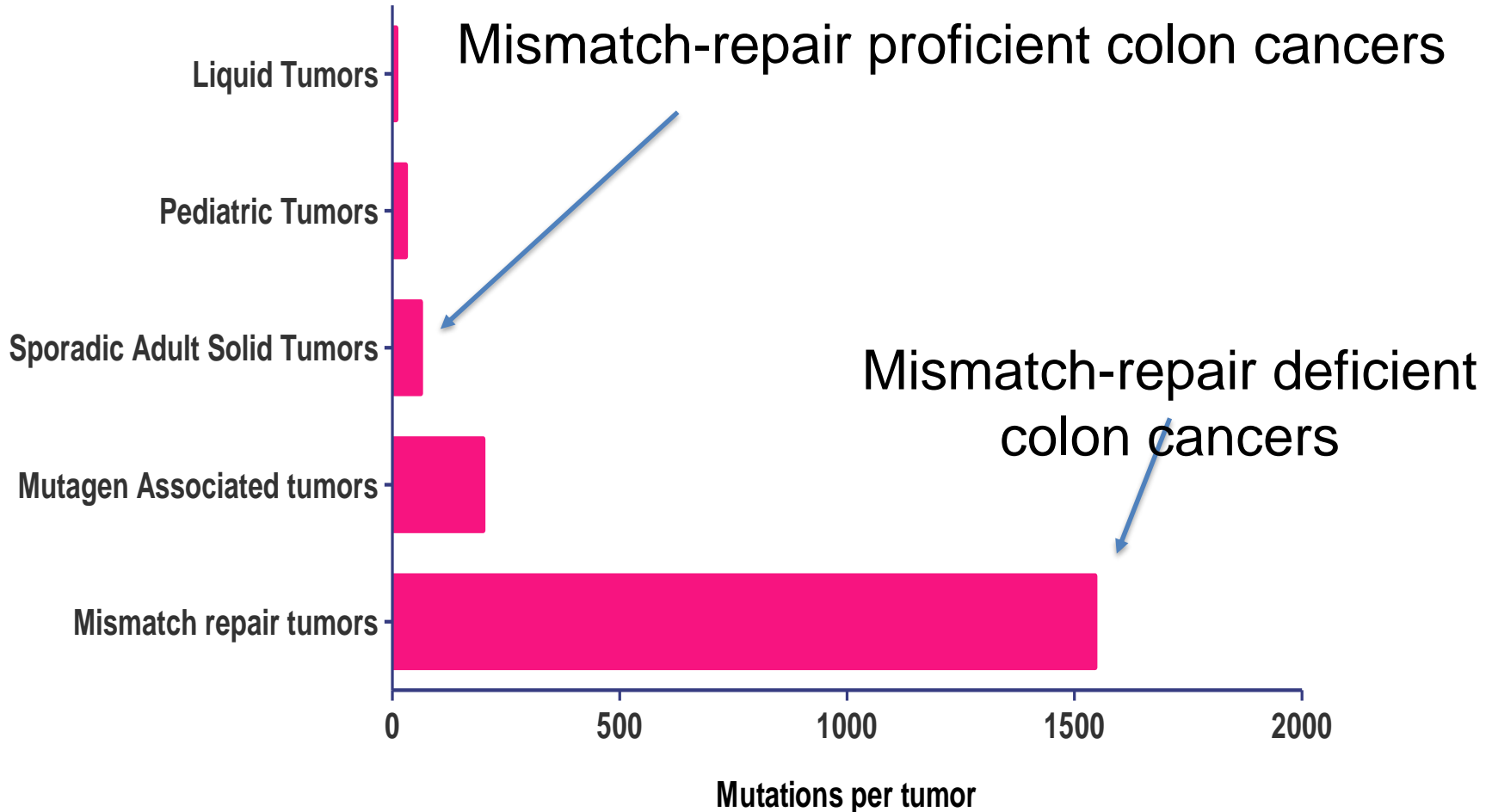
- Options for your patients
- Used to be colorectal cancer patients only
- But not any more!



# Mutations per tumor



# Mutations per tumor



# Hypothesis

- Mutations have been shown to encode proteins that can be recognized and targeted by the immune system
- Immune augmentation with PD-1 blockade may be highly effective in mismatch repair deficient tumors

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## Drugs

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**Approved Drugs**

Hematology/Oncology (Cancer)  
Approvals & Safety Notifications

# FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication

# May 23, 2017

# Pembrolizumab - Indication

- MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
- Other solid tumors
  - Unresectable or metastatic
  - MSI-H or dMMR solid tumors
  - Progressed following prior treatment
  - No satisfactory alternative treatment options



# Data

- 149 patients with MSI-H or dMMR cancers
- Five uncontrolled, multi-cohort, multi-center, single-arm clinical trials
- 90 patients had colorectal cancer
- 59 patients one of 14 other cancer types
- Objective response rate was 39.6%
- Responses lasted six months or more for 78% percent of those who responded
- Similar irrespective of whether patients were diagnosed with CRC (36%) or a different cancer type (46% across the 14 other cancer types).

# Precision Medicine

- Pembrolizumab and MSI/dMMR solid tumors
- The only real example of Precision Medicine
- Any cancer -> specific target -> specific drug
- Other examples of targets always depend on the histology or site of the tumor



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## Drugs

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### Approved Drugs

[Hematology/Oncology \(Cancer\) Approvals & Safety Notifications](#)

[Drug Information Soundcast in Clinical Oncology \(D.I.S.C.O.\)](#)

[Approved Drug Products with Therapeutic Equivalence Evaluations \(Orange Book\)](#)

# FDA grants nivolumab accelerated approval for MSI-H or dMMR colorectal cancer

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On July 31, 2017, the U.S. Food and Drug Administration granted accelerated approval to nivolumab (OPDIVO, Bristol-Myers Squibb Company) for the treatment of patients 12 years and older with mismatch repair deficient (dMMR) and microsatellite instability high (MSI-H) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

# Nivolumab

- MSI-H/dMMR metastatic colorectal cancer
- Progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- Study CA209142/CHECKMATE 142
  - Multicenter, open-label, single arm study conducted in 53 patients
  - The objective response rate 28%
  - Responses lasted 6 or more months for 67%

# Toxicity

[Ugeskr Læger](#). 2017 Oct 2;179(40). pii: V05170365.

**[Immunotherapy is cancer treatment with a novel side-effect profile].**

[Article in Danish]

[Kondrup M<sup>1</sup>](#), [Raunkilde L](#), [Svane IM](#), [Schmidt H](#), [Bastholt L](#).

- Different from other anti-cancer drugs
- May arise late and after end of treatment
  - Skin
  - Gastrointestinal
  - Hepatic
  - Endocrine
  - Pulmonary

# Options in Denmark

- Prevention
  - None
- Adjuvant
  - None
- First line metastatic, colorectal
  - Randomized phase III
- Last line metastatic, all MSI-H/dMMR
  - Phase I-II
  - Individual

# First-line treatment

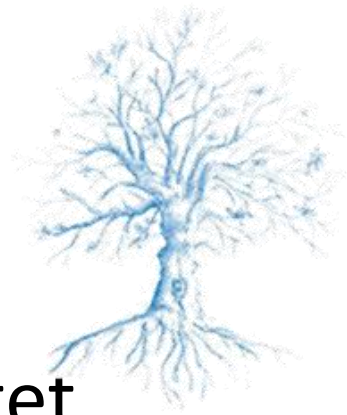
- Keynote 177
- Immunohistochemistry or DNA MSI
- Essential to identify patients at the MDT conference
- Herlev
- Odense
- Vejle

# Last line

- Some other tumors
  - Keynote 158, pembrolizumab
  - Other basket trials or phase I
- Predictive Value of Drug Sensitivity Testing Tumorspheres From Patients With Metastatic Colorectal Cancer (NCT03251612)
  - Phase II, 90 patients
- Ask for a second opinion



# What's New



- MSI-H/dMMR is the only druggable target across a spectrum of solid tumors
- Several treatment protocols available for your patients
- Individual options last-line