

Melanoma patient network Europe - Special conference for rare melanomas

Dear all,

from 19th of October until 21st of October was the MPNE conference for rare melanoma in Berlin. We had the opportunity to do a presentation about CMN, melanoma related to CMN and our organisations Naevus Global and Naevus International.

On the conference, there were 10 different sessions.

In the introduction, Bettina said, that rare melanoma should use the fully available network for melanoma and it's one of the main aims to raise the knowledge for patients and patients advocates.

She also introduced to their principles:

- Patients first.
- Solution, not problems.
- Data, not opinions.
- If you don't do it, no one will.

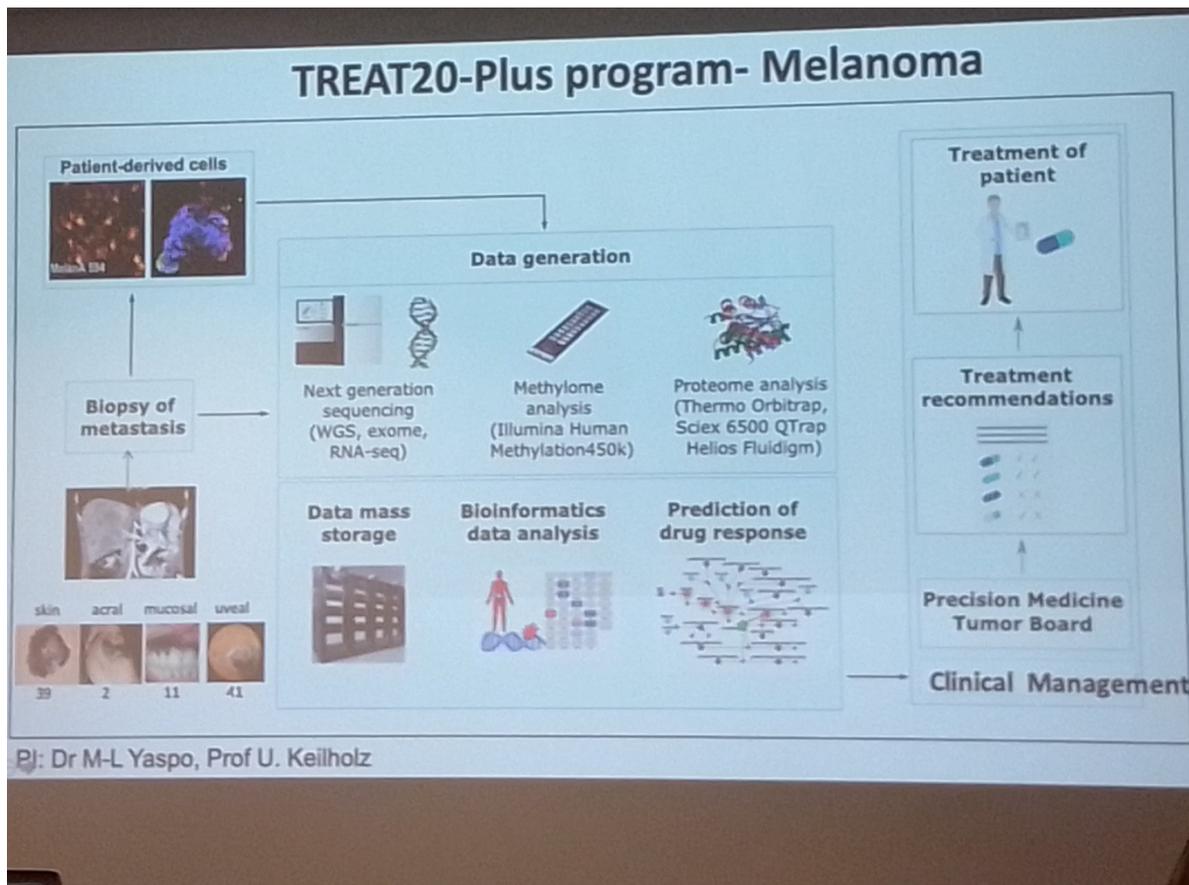
Session 1: "Thinking rare melanomas"

There was an explanation about: What is cancer and how does it start. In short, cancer is a disease of the genome because of mutations during the cell division. With help of DNA and RNA sequencing, 30.000 cancer genomes are already sequenced with 711 known cancer genes and 1661 additional candidates.

In the other part, they talked about germline mutations in uveal melanoma. Uveal melanoma is a cancer, that arises in the uvea, which is a pigmented layer of the eye. In most cases for the BAP1-TPDS (tumor predisposition syndrome) it's somatic, but sometimes it's a germline mutation. For BAP1-TPDS, there are also some cases of cutaneous melanoma.

Session 2: "Precision medicine in rare melanomas at Charite Berlin"

On this session, they explained the Treat20+ program for melanoma and how it is used for uveal and mucosal melanoma. Mucosal melanoma occurs on mucosal surfaces of the body, lining the sinuses, nasal passages, oral cavity, vagina, anus and other areas.



Treat20+ is an experimental personalized medicine program for metastatic melanoma. It's focused on prediction of drug response.

Session 3: "Essential anatomy"

In this session, they showed the anatomy of the eye and where uvea melanoma can occur. Also they explained about UMCURE2020, which is a project from clinical ocular oncology and basic research with patient organisations to develop new therapeutic approaches to treat uveal melanoma.

After the session, there was a World Cafe reception with a brainstorm to reduce the impact of all affected melanomas at the conference in term of prevention, early detection, treatment and survivorship. The aim was not just to be alive, it was on focus to live best possible.

Session 4: "Paediatric and familial melanoma"

On Saturday, they started with paediatric and familial melanoma.

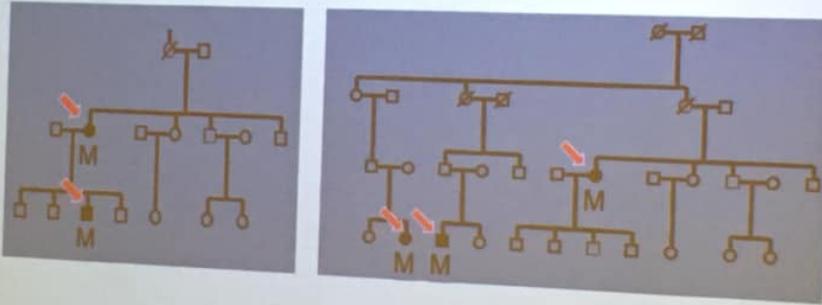
The first presentation was about familial melanoma and the genomel initiative.

Around 10% of the genes are familial melanoma for cutaneous melanoma. Familial melanoma means, they are inherited mutation, because they are in all cells of the body. There is a 50% chance to pass over the mutation to offspring during each pregnancy.

Search for melanoma genes: research starting position 1989

Melanoma in two first degree relatives

Melanoma in ≥ 3 family members



One of the melanoma genes called CDKN2A on chromosome 9. CDKN2A mutations are in 40% melanoma families worldwide. The risk to developing a melanoma, when you are a carrier of a mutation in CDKN2A gene is 70%.

What about the moles and carriership?

Mutation carrier



Non-carrier



Moles do not predict mutation carrier status.

When to visit a clinical geneticist (NL)?

A family with:

- 3 members with melanoma (of which 2 first degree)
- 2 members with melanoma and 1 with pancreatic carcinoma

A person with:

- 3 or more melanomas
- melanoma < 18 years of age
- with melanoma and pancreatic ca. or cancer in the mouth/throat

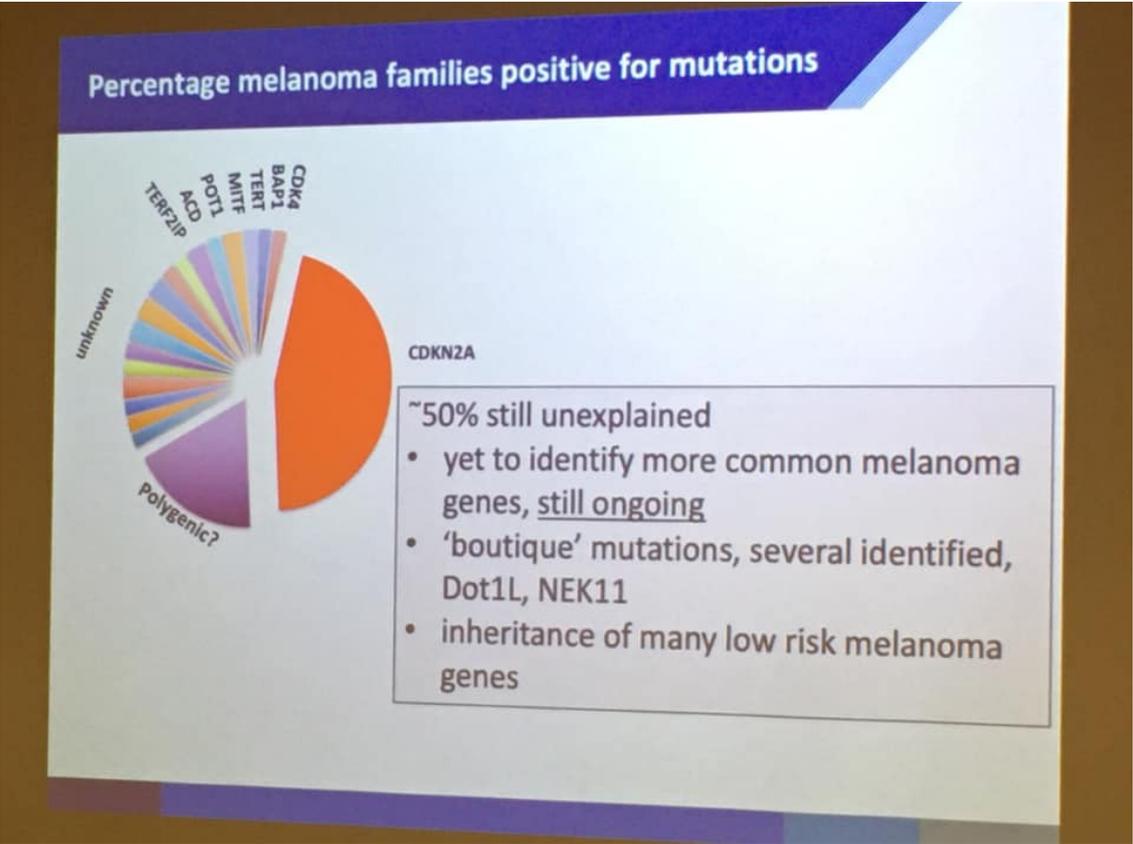
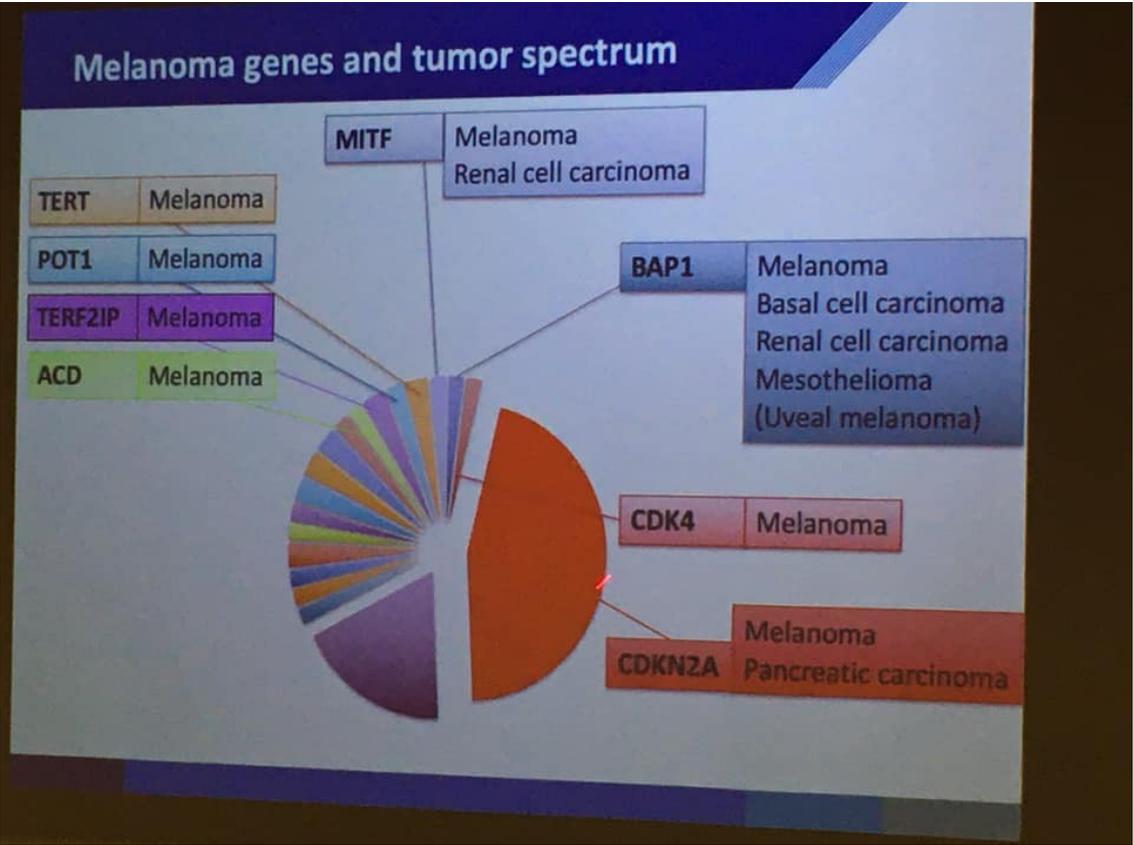
What if you are having a mutation in CDKN2A (NL)

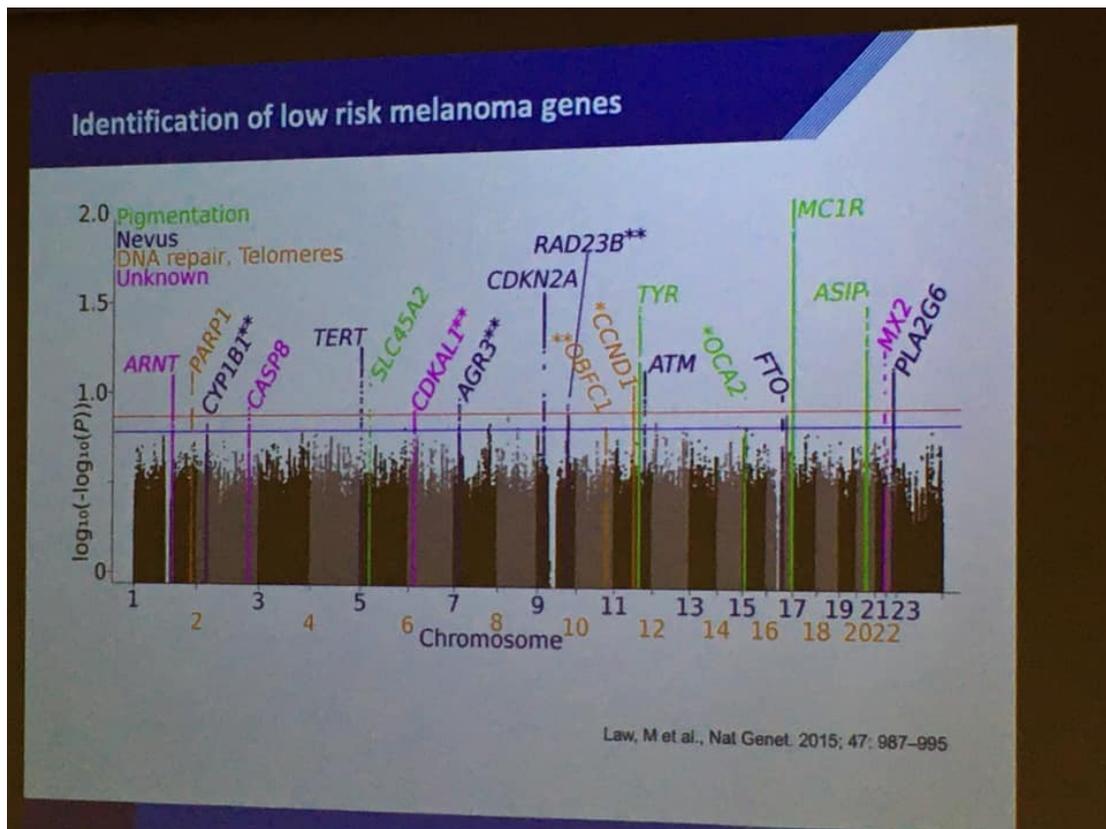
Mutation carrier:

- (healthy) family members can be tested
- 18+ half yearly skin control
- 45+ yearly MRI pancreas
- adapt your life style: careful in the sun, do not burn, stop smoking,
- child wish: *in vitro* fertilization combined with pre-implantation genetic diagnostics

Halk AB et al. Surveillance for familial melanoma: recommendations from a national centre of expertise. Br J Dermatol. 2019 Sep;181(3):594-596. doi: 10.1111/bjd.17767. Epub 2019 May 1. PubMed PMID: 30742720.

Treatment of familial melanoma is similar to sporadic melanoma. Immuno-therapy seems to work better in case of familial melanoma.





About GenoMEL:

GenoMel is a melanoma genetics consortium for researching and sharing information about familial melanoma.

GenoMEL: www.genomel.org

GenoMEL: The Melanoma Genetics Consortium

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- Identification new melanoma genes
- Study gene-environment interactions
- Study gene-gene interactions
- Educate physicians and patients

News | August 2017
 The second UK Melanoma Patient Conference

News | July 2017
 How we in Leeds access on-going healthcare data about our research participants

News | June 2017
 Launch of Patient Decision Aid

News | June 2017
 Melanoma Focus

GenoMEL database

| GenoMEL database | No. of Families | Total no. of Participants | No. affected members with melanoma | Residence calendar completed | Sun exposure completed | Phenotyping completed | CDKN2A genotyping completed |
|------------------|-----------------|---------------------------|------------------------------------|------------------------------|------------------------|-----------------------|-----------------------------|
| Total | 1517 | 9435 | 2300 | 3664 | 2111 | 1808 | 3018 |



Current GenoMEL Aims:

- Design of prediction models CDKN2A carriership
Taylor NJ, et al. J Am Acad Dermatol.2019;81:386-394.
- Design prediction models based on high and low risk genes and/or phenotypic characteristics- ongoing

GenoMEL
The Melanoma Genetic Consortium

What is the chance that you have inherited a mutation in CDKN2A?

10/2016, Heston and colleagues developed a simple online model - called MEL.PREDICT - that predicts whether or not an individual carries a mutation in CDKN2A. Qualification for this model requires three pieces of information to provide maximum utility:

1. Age at first diagnosis with melanoma
2. Total number of primary melanoma diagnoses
3. Number of additional family members with melanoma

Recent work by GenoMEL, the international melanoma consortium, showed that these three variables were important predictors of CDKN2A status using melanoma gene families from across the globe. Having a personal or family history of primary cancer also may be important predictors of CDKN2A status (under review).

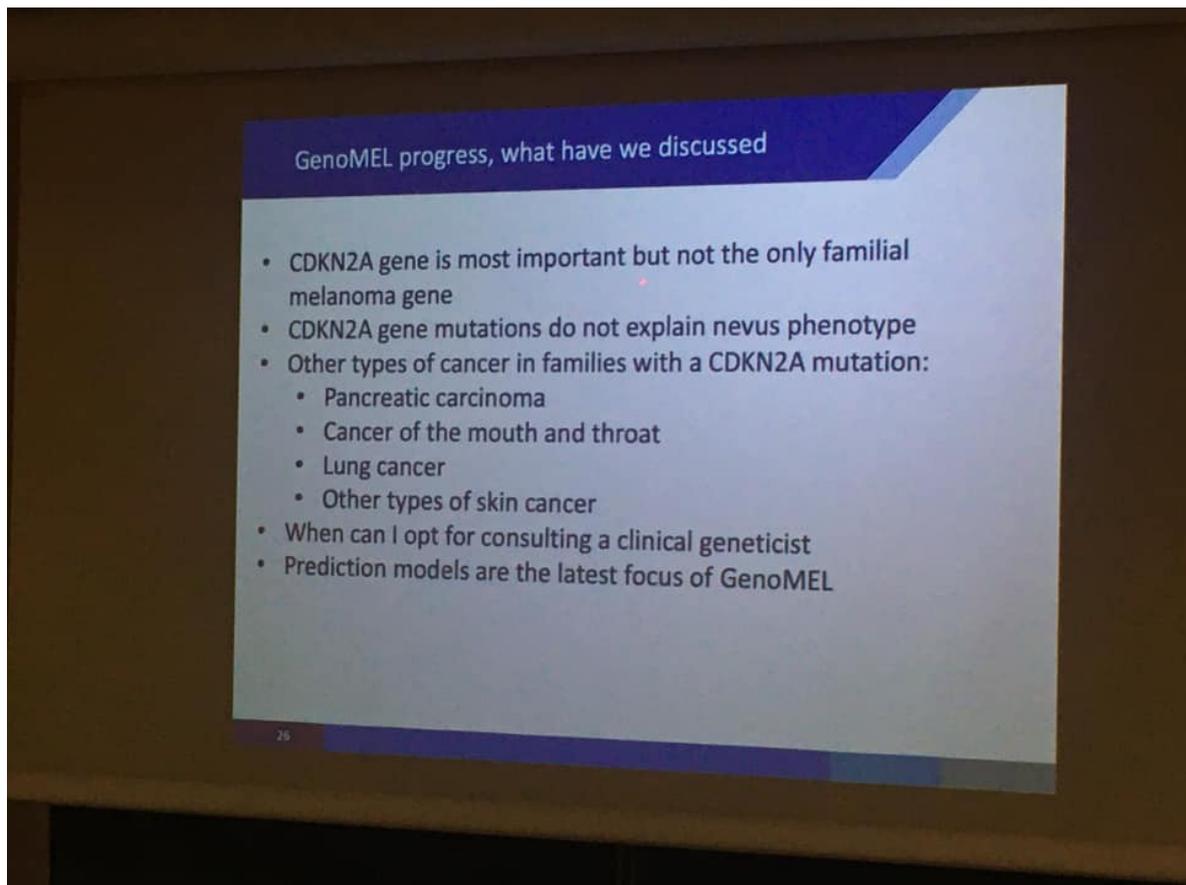
By answering the questions below and clicking the submit button, you will receive a percent as a range of percent, indicating the probability that you carry a CDKN2A mutation.

Q1. How old were you when you were first diagnosed with melanoma?

Q2. How many primary melanomas have you had?

Q3. How many other members of your family have been diagnosed with melanoma?

Q4. Have you or any of your family members been diagnosed with genetically cancer?



The next presentation was about us. Like said before, we had the opportunity to do a presentation about CMN, melanoma related to CMN and our organisations Naevus Global and Naevus International.

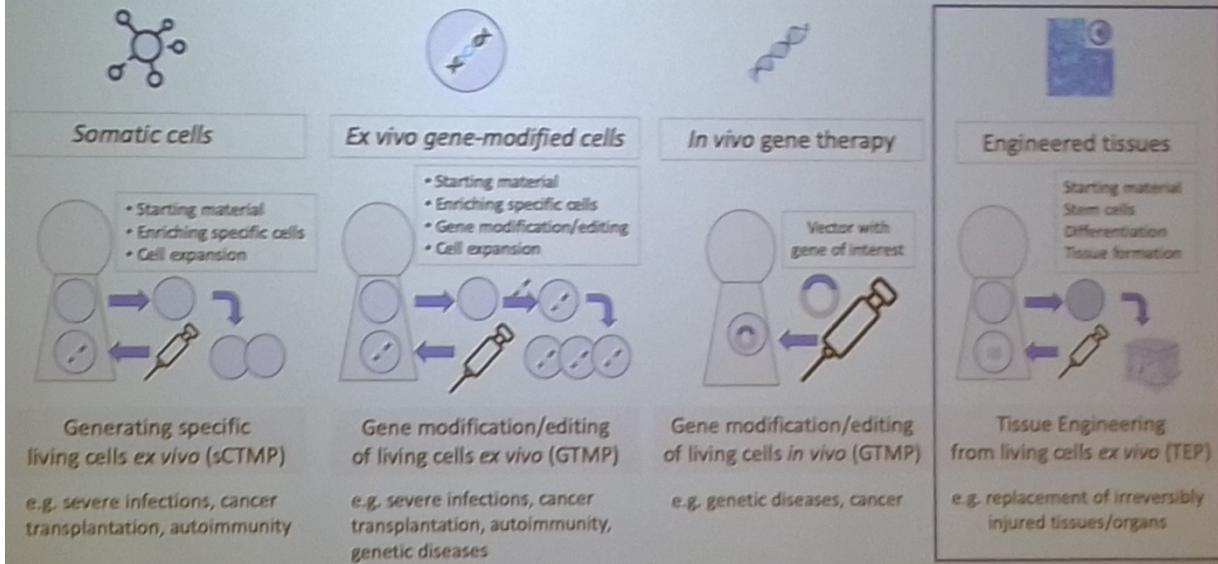
Session 5: "Primary ocular melanoma and prognostication" and Session 6: "Treatment metastatic uveal melanoma today"

Session 5 and 6 was all about ocular / uveal melanoma. So what occurs the risk, what kind of prevention, early detecting and treatment is possible.

There was a presentation about "Restore horizon" and "living drugs". Here is a overview on Youtube: <https://youtu.be/f44xYZDPS30>

They said, it is already in use. There were around 1800 treatments already in 2019. They showed some promising skin transplantations. If they can deliver, what they promise, this might be a possible treatment solution in much cases for us.

Advanced Therapies – „Living“ Drugs



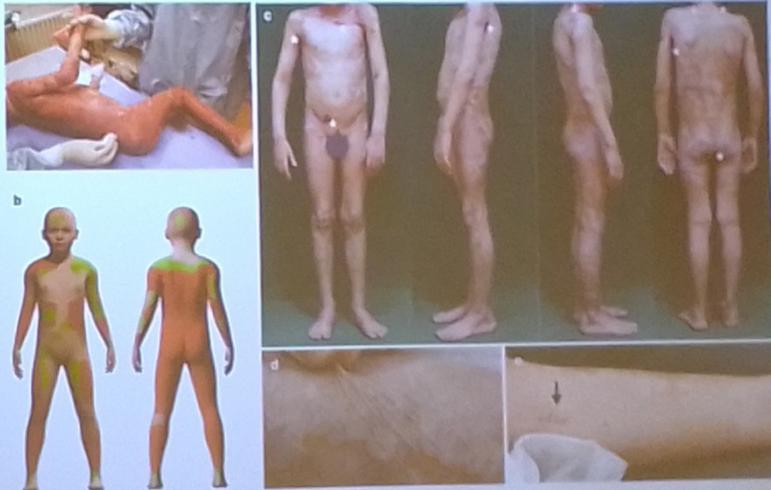
RESTORE

RESTORE - Health by Advanced Therapies

Advanced Therapies – not just a dream, it is already “reality”

nature
International journal of science

Dieter Hirsch [...] Michele De Luca (2017)
Generation of the entire human dermis using transgenic stem cells



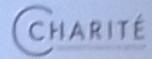
Junctional epidermolysis bullosa

2 years later

RESTORE

RESTORE - Health by Advanced Therapies

Reshape undesired immune reactions by Treg cells



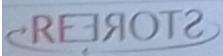
Male patient, 9 yrs
 Stem cell transplantation 11/2013
 Development of acute GvHD => β -Thalassemia major
 10/10-ident MRD-PBSC
 Progression to therapy-refractory chronic GvHD



09/2015: Single shot Treg therapy (donor derived) => rescue within few weeks, long-lasting benefit



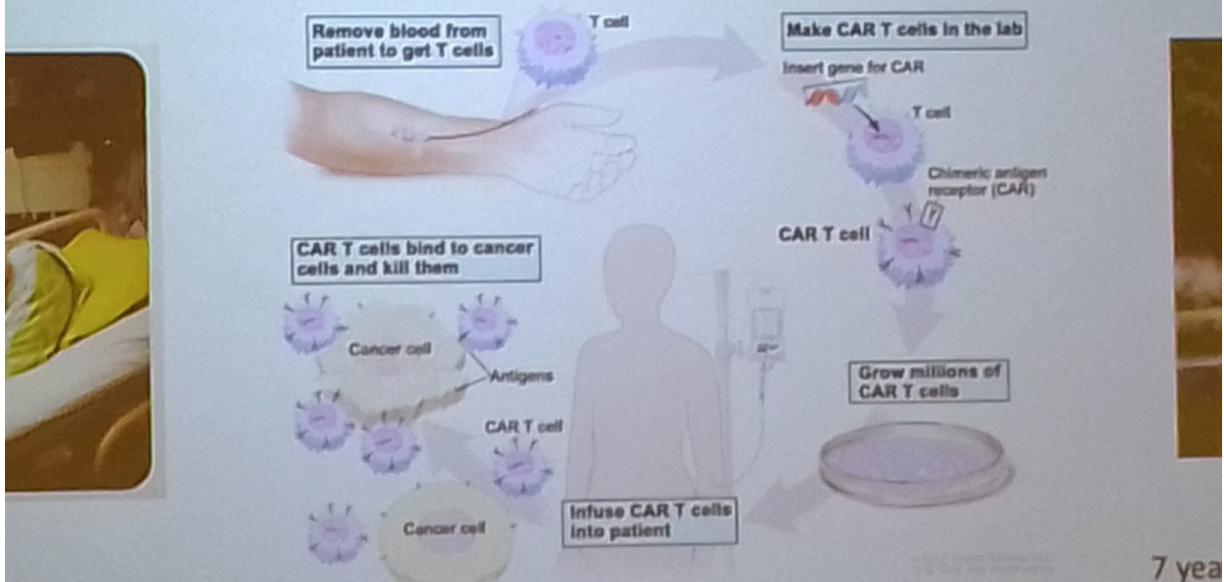
Landwehr-Kenzel S
 Eggert A ...
 Reinke P
 in preparation



RESTORE - Health by Advanced Therapies

store anti-cancer immune response by redirecting T cell

CAR T-cell Therapy



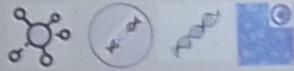
Redirecting T cells
 and amplify the pool

7 yea
 Fr

Advanced Therapies are a **reality**, but only a **few** patients benefit from them so far

No Fiction – already Reality

There are **Cures** by Advanced Therapies



- ⇒ Genetic diseases
- ⇒ Immune diseases
- ⇒ Cancer
- ⇒ Tissue Repair

The ISSUE

Few products on market only,
Few patients benefit so far

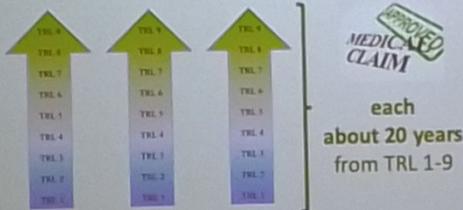


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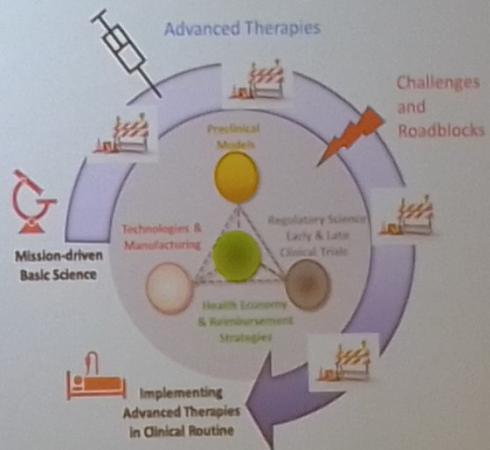
Why are only few Advanced Therapies implemented so far ?

Why ?

- ⇒ Long and costly added value chain
- ⇒ Final product: high costs of goods



“Living” drugs are a Disruptive Innovation
challenging the “tried and tested” paradigm
⇒ obstacles & roadblocks abound

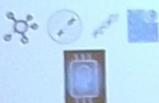


Need for broad networking

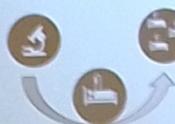
Life Science Community



Transdisciplinarity

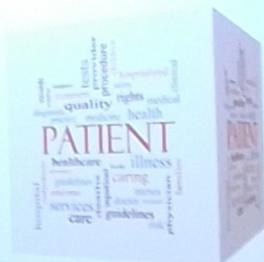


Technology

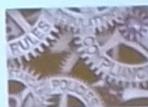


Translation

Alliances with Patients,
Patient Advocates &
General Practitioners



Regulatory, Ethical &
Health Economic Issues



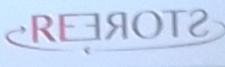
Regulatory Science

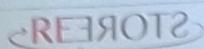


Ethics Science



Health Economics
Science

Aimed by 



RESTORE - Health by Advanced Therapies

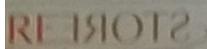
The Vision

RESTORE health to chronic diseases by "Living Drugs"

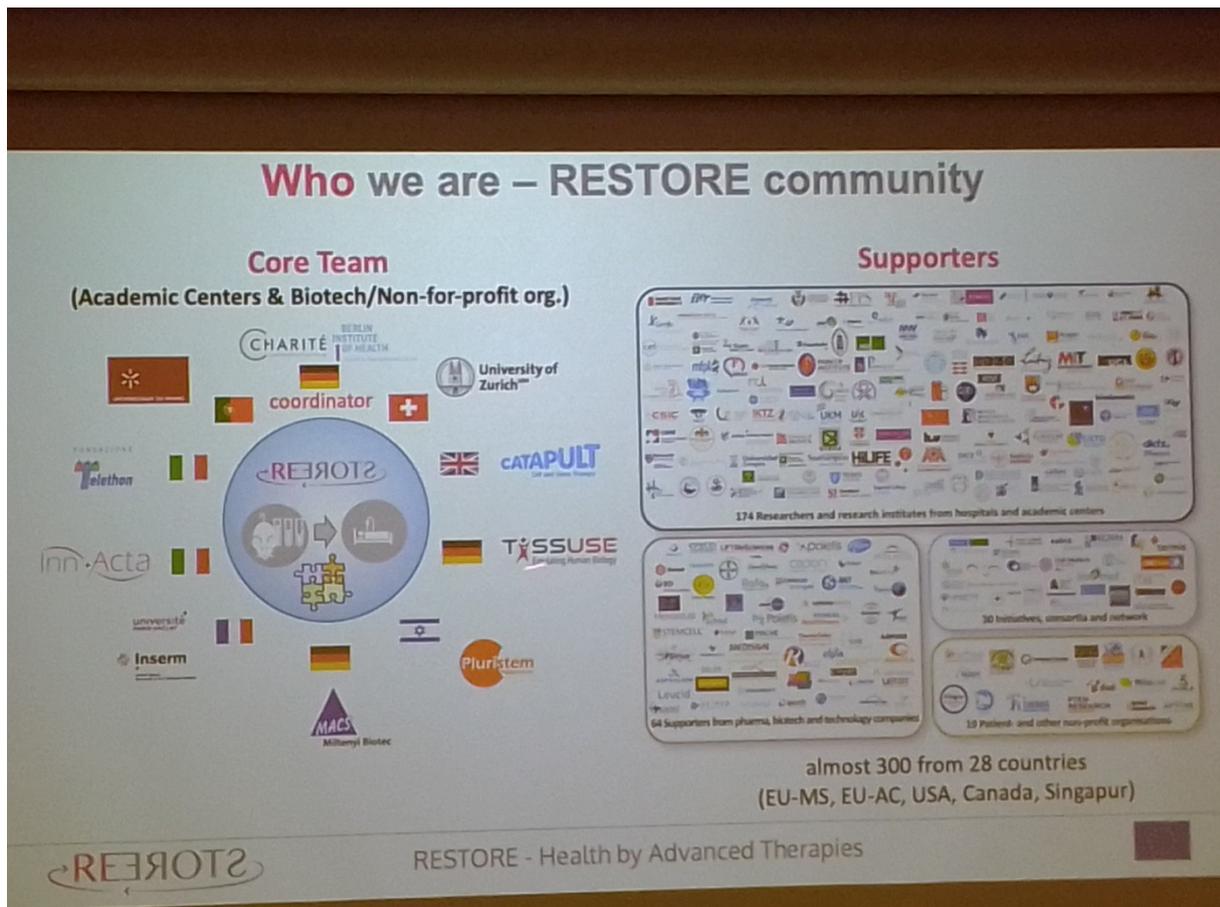
- Make the disruptive promise of Advanced Therapies a reality to **cure** chronic diseases
- Make Advanced Therapies accessible as **"standard-of-care"** for every European patient in need
- Make Europe a **spearhead** of Advanced Therapies in **Science, Clinics and Biomedical Industry**
- Make use of the enormous **socio-economic potential** of novel breakthrough-therapies also in Europe

The Mission

- Overcome the **technological and regulatory roadblocks** for Advanced Therapies in Europe
- Deliver a pipeline of **dozens of revolutionary AT products** "developed and made in Europe" by 2030
- Establish a **sustainable pan-European ecosystem** integrating research, clinics, industry and patients



RESTORE - Health by Advanced Therapies



<https://www.restore-horizon.eu/>

Session 7: "GNAQ/11 mutations"

GNAQ/11 is a driver mutation gene in choroidal nevus for uveal melanoma. Something that this might cause is blue lights from Smartphone, Television, Computerscreen, artificial light etc.

Session 8: "Mucosal melanoma"

This session was about mucosal melanoma, about the locations, where it occur, what kind of symptoms will be there. They showed studies with current drugs, but the studies doesn't look very promising.

Session 9: "Return of data sharing and how patients benefits from their own data"

This was a very interesting session about data usage for patients and patient support groups. We got introduced to the FAIR principles (<https://youtu.be/K40utIzUzOk>).

Findable

Accessible

Interoperable

Reusable

Datas are worth a lot of money these days. If the patients/advocates would have the data, they have the advantages with their data, about data sharing for what they care, the political and media influence, which gives them power.

The Duchiness organization (<https://worldduchenne.org>) started to collect the datas. They found out, that 80% accumulated health data is lost in 2 years and 30% of healthcare costs are bad data related. They have connection to someone from Microsoft(?), who helping them and said, they should stop sharing data. So they started a "health train" that is an ICT infrastructure, based on the FAIR principles that facilitates data visiting instead of sharing. to change the role of the patient and becomes a powerful privacy by design enabler.

With a registry, the want to bring together the data and want to connect them with medical research, clinical care/trials and each other.

Session 10: "Advocacy session"

Sunday was the advocacy session. It was shorter than planned, because we used the morning for Session 9, that was originally planned for Saturday.

On part was about clinical trials outside of the own country. It's the best option if there is no effective standard of care, sometimes the only option. There is a website, where you can look for trials:

The image shows a screenshot of the ClinicalTrials.gov website. At the top, the title "How to find clinical trials" is displayed. Below it, the URL <https://clinicaltrials.gov/> is highlighted. The website header includes the NIH logo and the text "U.S. National Library of Medicine". A navigation menu contains links for "Find Studies", "About Studies", "Submit Studies", "Resources", and "About Site". A purple banner states: "ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world." Below the banner, there is a section titled "Explore 319,841 research studies in all 50 states and in 209 countries." followed by a disclaimer: "ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine. IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details. Before participating in a study, talk to your health care provider and learn about the risks and potential benefits." The main search area is titled "Find a study" and includes a "Save Studies (X)" button. It features several search filters: "Status" with radio buttons for "Recruiting and not yet recruiting studies" and "All studies" (selected); "Condition or disease" with a text input field and a clear button (X); "Other terms" with a text input field and a clear button (X); and "Country" with a text input field and a clear button (X). At the bottom of the search area, there are "Search" and "Advanced Search" buttons. The footer contains links for "Help", "Studies by Topic", "Studies on Map", and "Directory".

Conclusion:

I think it's worth to attend to MPNE. The problems in general are similar to the problems of CMN and other rare diseases, so we are in one boat. There are probably correlations between CMN melanoma cases and cases between the other rare melanomas, but that's a job for the researcher/scientists.

Not sure about BAP1 and GNAQ/11 mutation. The restore horizon initiative sounds very promising, when we talk about skin transplantation for large and giant nevi and also for cases for skin melanoma, but not sure about neurological melanoma.

Another very interesting part that might be important for us, is what the Duchiness organization is doing with their data collection of their disease affected people. We can get a huge profit out of it.

Bettina talked a little bit about Horizon 2020 and the project out of it share4rare. This might be an ability to get funds for Naevus International and Naevus Global, but this require more infomations.

And i think it might be an idea to contact (skin) melanoma organizations, because there is a possibility to get in touch with other CMN affected people.