The KI program for Personalised Cancer Medicine (PCM).
Participation of groups/PIs in basic biomedical cancer research

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BACKGROUND

The emerging sequencing technologies of the 21st century has allowed the mapping of cancer cell genomes, transcriptomes and proteomes, leading to a fine sub-classification of tumor types and to the discovery of diagnostic, predictive and therapeutic targets. Further, molecular technologies for manipulation of gene expression in eukaryotic cells has contributed to the understanding of the biologic relevance of these biomarkers. With the addition of multiplexing image technologies for visualization of proteins in situ, the architecture of normal and malignant human tissue proteomes have been generated.

These types of analyses are gradually being adopted in routine diagnostics and the information generated is used for cancer group classification and to define individual genetic and phenotypic landscapes.

However, relatively few biomarker discoveries have been adopted successfully into the treatment of cancer patients and the translation from basic cancer research to patient treatment is still lengthy and challenging.

OBJECTIVES

The aim of the present investigation was to make a survey among basic researchers to define their level of commitment in personalized cancer medicine (PCM) research and to identify the gaps they experience translating basic research into clinical applications.

GROUP AND METHODS

Researchers from Karolinska Institutet were selected by the following criteria: Principal Investigators, Basic Researchers, non clinicians, balanced gender, representing KI campus, KI Solna, KI Huddinge, and SciLifeLab. Twenty researchers, were interviewed (10 female + 10 male).

The method consisted of personal interviews with the researchers.

The interview consisted of 8 questions previously elaborated by the PCM-reference and steering groups.

Questionaire

1. What is your current understanding about personalised/precision cancer medicine (PCM)?

2. What is your view on PCM as a future therapeutic concept for cancer?

3. Are you working with human cancers? Which type? Do you have contacts or collaborations with clinicians with expertise or managing patients with the type of cancer you do research on?

4. Does any part of you current or planned research address issues related to personalised cancer medicine? Do you identify possible biomarkers relevant for prognosis and/or choice of therapy? Do you identify possible targets for treatment? Do you develop new therapies?

5. Are you aware of the KICancer Diagnose based groups?

6. Are you aware of the PCM program at KI? Would you like to be involved? In what way? What are your strengths.

7. Do you think there is a need for a PCM network in Stockholm/Sweden? Why?

8. Are there any "workflow obstacles" for your group to be involved in translational PCM research at KI/Stockholm?

RESULTS

1. What is your current understanding about personalised /precision cancer medicine (PCM)?

The majority of the interviewed researches have a concept of precision medicine based on the genotypic and phenotypic characterization of individual patient tumors for treatment decisions. "treatment" and "genotypic characterization" were key words. Few commented on the phenotypic characterization (i.e drug screening) as a tool for PCM.

Some individual definitions of PCM:

-Rational cancer treatment based on the molecular profile of patient tumors.

-Tailor-made treatment based on genetic characterisation of individual tumors.

-Matching patients genetic profiles with therapy.

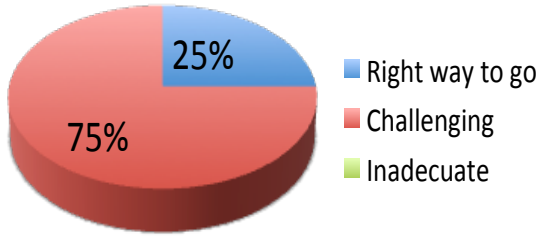
-Precision medicine is not diagnostic but diagnostic may be needed.

-Right treatment to right patient.

- PCM concept may have a function but can be deteriorating for basic research.

-The word “Personalised” should be change for “comprenhensive”

2. What is your view on PCM as a future therapeutic concept for cancer?



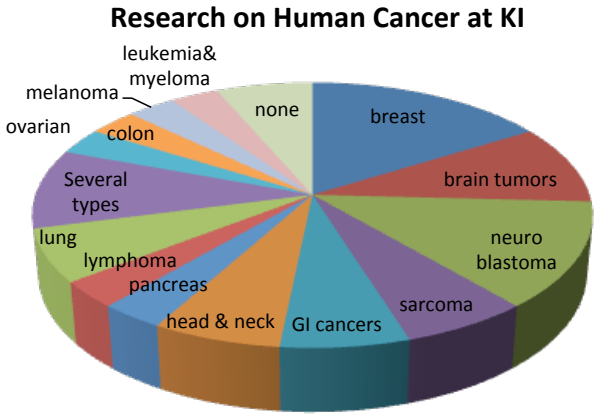
Seventy five percent of the researchers expressed weather precision medicine is the right way to go to cure cancer in the future. However, they do not disregard the potential of this approach of improving cancer treatment and survival of patients.

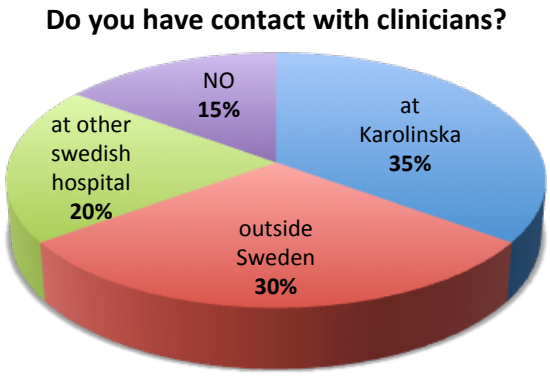
Challenges for PCM

a) The complexity of cancer, e.g. intra-tumor and inter-tumor heterogenity.
b) Only 127 genes are mutated in cancer and few have actionable mutations. There is a need for new approved drugs.
c) PCM has a potential but we need to understand tumor biology.
d) PCM can not be applied to all cancer patients.
e) The costs of new treatments will be a bottleneck for clinical implementation.
f) PCM is a modern concept. We need long-time visions in cancer research.
g) The funding support of PCM projects on behalf of basic research projects can have deteriorating consequences for basic cancer research

3. A) Are you working with human cancers? B) Do you have contact with clinicians?

Three of 20 researchers have projects that are only related to method development and do not involve a particular cancer type. Ninety percent of the researchers have projects on a broad type of human cancers. Of note is that several researchers work with different human cancer models.





4. Does any part of you current or planned research address issues related to PCM?

The majority of the basic cancer researchers were not directly involved in precision medicine projects however, they pointed out that their research can lead to novel treatment options and that this is fundamental for the development of new therapies. No new therapy can emerge without basic science.

The areas of research of the investigators at Karolinska Institutet were in the following groups:

a) Basic research with potential PCM connection.

b) Biomarker discovery.

c) Prognostic and predictive markers.

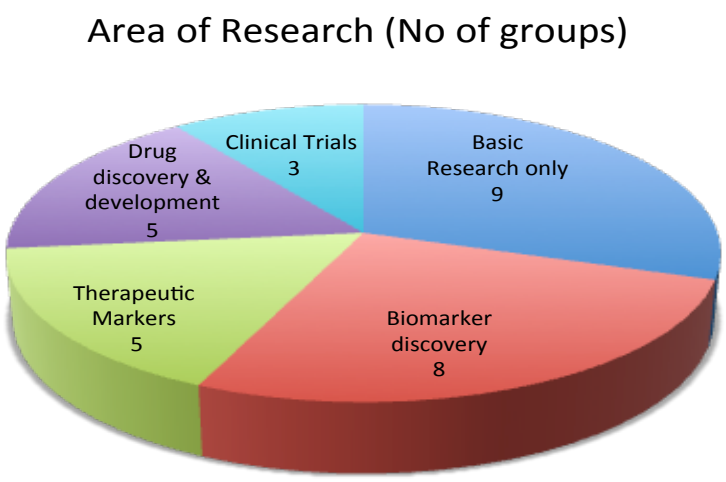
d) Therapeutic markers.

e) Drug discovery and Development.

f) Clinical trials.

g)

Note: Many groups perform research in different disciplines. All groups do basic research but only nine do it exclusively.



5. **Are you aware of the KICancer Diagnose based Groups?**

   15 groups of 20 (75%) were aware of the diagnose based groups at Karolinska

6. **Are you aware of the PCM program at KI?**

   Seventy percent of the groups (14) were aware of the PCM program at Karolinska. Six groups were not aware of the initiative.

   b) Would you like to participate?

   Most groups would like to participate but they wanted to know more about the initiative: the goals, the organization and the possibilities for funding.

   There was an interest of being engaged in concrete translational projects where the PI´s research could be implemented into clinical research.

   c) What are your strengths?

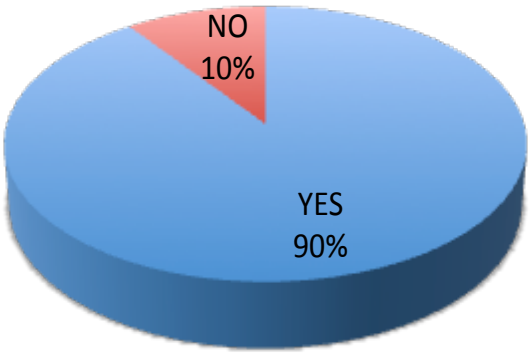
   There exists a broad and excellent competence among cancer researchers at Karolinska. Some of the projects were already multidisciplinary and are moving to the clinic.

   The areas of competence were:

Competence of the group	
PI	**Competence**
1	Drug discovery and development, “investigational”.
2	Technology: single cell sequencing. Mutation analysis in single cells.
3	Mouse models for metastatic cancer.
4	Drug discovery and development.
5	DNA repair, RNA biology.
6	Basic cancer biology, animal models of cancer.
7	Robust experience on NGS on tumor material.

8	Multidisciplinary network, fusion gene biology.
9	Expertise in infection biology, cancer and immunology.
10	Drug development skills.
11	In situ single cells methods.
12	Innovation, good ideas.
13	Basic cancer biology.
14	Competence. Candidate compounds that are patented. Drug development.
15	Predictive markers.
16	Molecular knowledge and technologies: ChiPseq.
17	Cell and tumor biology, differentiation. Techniques.
18	Expertise in biomarker discovery.
19	Drug development
20	Cell metabolism and drug discovery

7. Do you think there is a need for a PCM network in Stockholm, /Sweden?



The majority of the groups, 18/20, were positive to the PCM initiative. They expressed that Karolinska is an excellent place to bring basic and clinical cancer research together to improve patient care. The PCM initiative should be inclusive and requires excellent leadership. PCM should be supported only if it delivers results.

Two groups were negative towards this concept. They pointed out that big efforts have been done for biomarker discovery over the years but few of them have reached the clinic. There already exist cancer networks at Karolinska such as StratCan, KI-Cancer. Bring them together.

8. Are there any "workflow obstacles" for your group to be involved in translational/PCM research at KI/Stockholm?

In general, there was a consensus regarding the existence of a big gap between preclinical and clinical research. They expressed that KI has a fantastic

infrastructure but needs to be canalized with a vision. Today research at Karolinska is fragmented. The gaps can be summarized as follows:

a) Difficulty to find clinicians willing or able to collaborate with basic researchers.

   This was a common opinion among many researchers, pointed out by 14 of 20 interviewed fellows. They experienced that it is difficult to find clinicians that have time and interest to engage in translational projects. This could be partly explained by the present organization of the Karolinska Hospital with increased patient work, and lack of time for research.

   It takes a long time to build up confidence in basic research among clinicians and within a multidisciplinary network. It is important to sustain networks that have taken many years to build-up.

   Several investigators expressed that they found it easier to collaborate with clinical departments in other parts of Sweden or abroad than at Karolinska.

b) Biobank resources

   In spite of the excellent resources at Karolinska with tissue and blood biobanks linked to patient registers, it remains complicated to get access to clinical material. Poor administrative resources and complicated ethical applications contribute to this deficit. Other University hospitals in Sweden have functional Biobanks, explaining partly the choice of collaborators outside Karolinska.

c) Data Sharing

   The research community could benefit from having access to data generated with new generation sequencing techniques. Today, there exist some open databases in the world. An excellent example is the Human Proteome Atlas. At Karolinska there exist projects where patients NGS data is being generated. Allow these databases to be available.

d) Clinical Trials

   Several groups run drug discovery and development projects and have identified and validated inhibitors with potential use for cancer treatment.

First-in-man trials are crucial for the clinical development of these compounds, and bridging the gap between basic research and clinical implementation is crucial. It requires extensive funding, clinical engagement and patients. Facilitate the possibility to perform first-in-man clinical trials at Karolinska.

e) Hierarchic Structure at Karolinska

There exist a hierarchic culture at Karolinska that has to be counteracted in order to benefit teamwork. Funding organizations should reward multidisciplinary work.

f) Big science is probably not going to deliver scientific breakthroughs. Basic research should not be neglected.

Conclusions.

There is common understanding for the concept of precision medicine among basic cancer researchers. The investigators believe that PCM has potential as a future cancer therapy approach but it will face several challenges due to the complexity of cancer, the challenges for applying PCM into the clinic and the costs of the treatments.

Karolinska has a powerful infrastructure and a fantastic bank of knowledge and technology among basic cancer researchers. These resources should be exploited and canalized towards effective clinical research.

There is a need to bridge basic research with clinical research to push PCM forward. The major gaps are related to the difficulties to collaborate with clinical teams at Karolinska, to a complicated burocrasy to access tissue samples, difficulties to access NGS technologies, and poor data sharing.

PCM is a modern concept. We need long-term visions in cancer research. PCM needs a vision, a good action program and a strong leadership.

Concrete Actions

1. Promote connections between clinical and basic researchers.
    - Add a link at KI-PCM or KI-Cancer website with information.

- Promotion of multidiciplinary interaction hubs and meeting points.
- Fund Diagnosed based groups.
- Funding organizations should reward team science.

2. PCM should work for data sharing. Open databases could give better opportunities to researchers.

3. Work for a more efficient Biobank organization.

4. Reinforce clinical trial units at Karolinska.