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Exceptional Responder Analysis Tool

ayusharma

View revisions

Organization: OncoBlocks

Abstract: Onco Blocks proposed a project Exception Responder Analysis Tool, a powerful tool for cancer which will distinguish between people who become sick and those remain healthy, between patients who respond to the treatment and those whose condition is worsen, between pathogens that cause outbreaks and those are harmless.

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1. Introduction

"First happiness is the fit body."

We are using lightning fast data transfer and computation to defining the new ways for better life. New technologies are evolving at every moment with the help of collaborative human efforts. On the other side we are suffered from diseases of unknown causes. Cancer is one of them. These diseases marking a question on the existence of our future generation.

"Cancer causes more death than AIDS, Tuberculosis and Malaria combined."

Genes are the building blocks of life. Technology are helping us to read the building blocks and advancing the understanding, thus diagnosis, treatment, cure and prevention of the diseases. Finding the 0.01% percent difference in the human traces of the 6 Billion genetic sequence is now possible. Our aim to build the new tools for analysis and research of these traces which will result out in the exact method of prevention and cure of the diseases.

Onco Blocks proposed a project Exception Responder Analysis Tool, a powerful tool for cancer which will distinguish between people who become sick and those remain healthy, between patients who respond to the treatment and those whose condition is worsen, between pathogens that cause outbreaks and those are harmless.

During GSoC, my task would be to develop an web based platform which provide analytic and analysis for the cancer diagnosis treatment cure and prevention according to the Exceptional Responders.

2. MOTIVATION - WHY ONCO BLOCKS?

"Over 20 thousand of people die of Cancer everyday"

Main aim of any software to solve real life problem and provide better ways of life. My father has medical background so it developed an interest in me towards the issues in medical & life sciences from my childhood.

Being an open source contributor, I am able to put my efforts for the development of the product which can help people. My passion and skills in web technologies provided me an opportunity to work on Exception Responder Analysis Tool Project through which I can really help mankind.

"Write Code, Save Life, Spread Happiness"

Recently I got selected for the **MIT Media Lab Design Innovation - India Initiative** under the Civic Innovation Track where I worked on an application **Blood Collective** - A community driven blood donation network to locate donors and receivers in real time.

While in summer I worked as GUI developer for **Spiffout Infomedia Pvt. Ltd.** https://spiffout.com . This is a web based project which connect consumers to business and provide customer satisfaction analytic.

MIT Media Lab initiative helped me to learn about the design synthesis of the problem with help of field trips, surveys, group discussion and teamwork . In Spiffout I learned about web frameworks and analytic skills.

I found Exceptional Responder Analysis project similar to my skill set and passion.

GSoC 2015: This is a platform which will help me to enhance my practicality in the circumstances of life challenges which can be solved by better and creative ideas.

3.OBJECTIVE

"Imagine getting survival rate of cancer treatment in seconds instead of days without owning a research lab."

Implementation of the web based platform to mining the cancer genomes of Exceptional Responders and analyse this data for the better treatment of the cancer patients.

The development of the project would cover following aspects:

- 1. Decrease the cost on research and increase the information.
- 2. Prediction of the patients who respond to the drug.
- 3. Prediction of diseases.
- 4. Forecast the treatment success rate.
- 5. Prediction of optimal treatment pathway.

4. CASE STUDY

I have done the case study of the project and made a video for the introduction in the basecamp group.

<iframe src="https://drive.google.com/file/d/0B3Rw4slBaBmXVTlrV0x6RExzWjA/preview" width="640" height="480"></iframe>

Exceptional Responders: These are the patients who uniquely respond to the treatment which is not effective to other patients.

Exceptional Responder Initiative: NCI has embarked on the Exceptional Responders Initiative to understand the molecular underpinnings of exceptional responses to treatment, primarily via chemotherapy. As a proof of principle, there was a search of NCI's Cancer Therapy Evaluation Program phase II trial database over a period of 10 years (2002-2012) in which about 100 cases were identified as a demonstration that the types of cases needed for the ERI did exist.

<u>Cancer Genome:</u> Human cell contains the ATCG genetic sequence which function the cell and responsible for the essential proteins, this genetic sequence changes and start to synthesize the protein responsible for the enlargement of the cell. This enlarged cell destroy the neighbour cells and results into the formation of the tumor.

Types of Cancer: There are more than 100 types of cancer but majorly 10 type of cancer is observed, as follows:

Skin, Lung, Breast, Prostate, Colorectal, Bladder, Melanoma, Lymphoma, Kidney, Leukemia

Cancer stages: There are 5 stages of cancer, as follows:

Stage 0 'In Situ'

Stage 1 'Localised Cancer'

Stage 2 & 3 'Regional Spread'

Stage 4 'Distant Spread'

Cancer Grades: Grading systems differ depending on the type of cancer. In general, tumors are graded as 1, 2, 3, or 4, depending on the amount of abnormality.

5. CHALLENGES & QUESTIONS

During the development of the project there would be some challenges and

- Q. What would be the analysis factors for the Cancer with respect to Exceptional Responder?
- A. Cancer would be analysed on the basis of the mutation occurred in specific genes.
- Q. How would I calculate the survival rate of the patient?
- **A.** Survival rate would be calculated with respect to exceptional responders. More the similarity in of the patient and exceptional responders, more would be the survival rate.
- Q. How would I calculate the similarity rate of exceptional responders and patients?
- A. Similarity rate would be calculated by the number of similar genetic mutations in the patient and exceptional responders.
- Q. How would I handle the REST API Data and design the tool architecture?
- A. I would use AngularJS, as a MVC platform for REST APIs and architecture.
- Q. As there would be large data manipulation and calculation on client side Javascript, How would I handle that?
- A. I would use Mozilla Local Forage to improve the offline access.

6. PROTOTYPE

I have developed a three prototypes of the application under the guidance of Dr. Ethan Cerami. It can be found here:

Web: http://ayusharma.in/exception-responder-proto/app/#/

Github: https://github.com/ayusharma/exception-responder-proto.git

Specifications:

1. **Single Patient Prototype:** This prototype is made for the data mining of a single patient. It shows the information of all the biopsies of a patient.

- 2. **Multi-Patient Prototype:** This prototype is the basic model to analyse the patient survival rate with respect to exceptional responders. It also include the mining section for the information of patient as well as exceptional responders.
- 3. **Insertion Deletion Prototype:** This prototype shows the statics of the homozygous, heterozygous and deletion of the pair of bases in the chromosome.

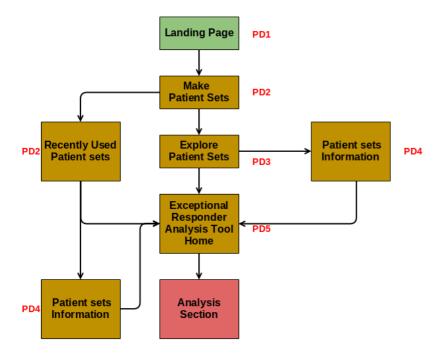
Other D3.JS Code Example: http://ayusharma.in/openhealth/

7. PROPOSAL DESIGNS

Design, a strategic roadmap which defines the specification, activities, plan and working of the system. I created visualization for the ERI tools.

DESIGN FLOW:

All the pages are represented in the following flow-chart along with their Code Symbol.



PD1. LANDING PAGE

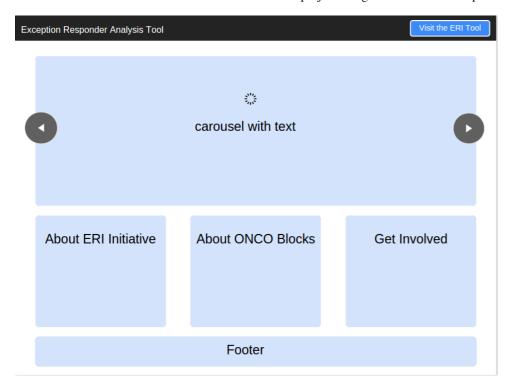
It will be the index page of Exceptional Responder Analysis tool. Information about the tool and the initiative would be mentioned here.

Carousel with text: An interactive carousel is to be designed, compromising the image set of the tool and cancer analysis.

About ERI Initiative: Information about Exceptional Responder Initiative is to be displayed here.

About ONCO blocks: Information about ONCO blocks is to be put here.

Get Involved: It will contain the documentation of the project along with detailed description to make contribution for project.



PD2. MAKING PATIENT SETS

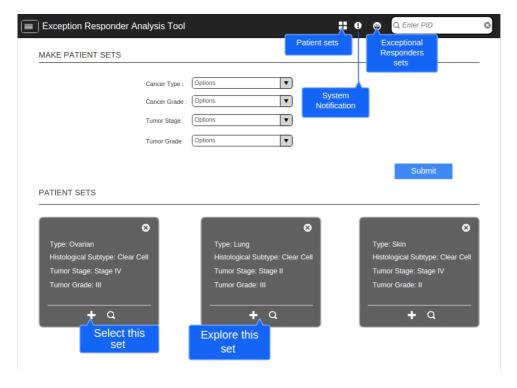
After visiting the home page user will come to the make patient set page.

Make Patient Sets: Interaction on this page will lead user to the formation of patient sets which would be categorised according to cancer types, grade, histology and stages.

Data Sets: This section will include the recent datasets on which user performed the operations.

Exceptional Responder Sets: It would be similar to the Data Sets.

Search Input: It would find the patient according to Patient ID.



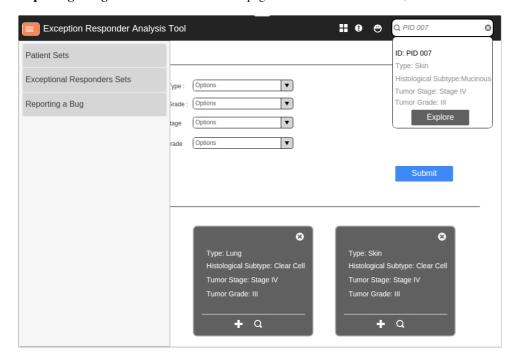
PD2. LEFT SIDEBAR:

Left sidebar would also be added to the system for upcoming addition of menus and integration.

Patient Sets: It would show all the sets present in the database according to type, stage grade and sub type.

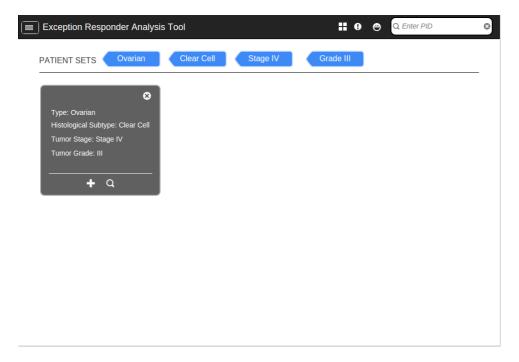
Exceptional Responder Sets: It would show all the sets present in the database.

Reporting a bug: It would direct user on a page user can submit the URL, Screenshot and information of bug.



PD3. EXPLORE PATIENT SET

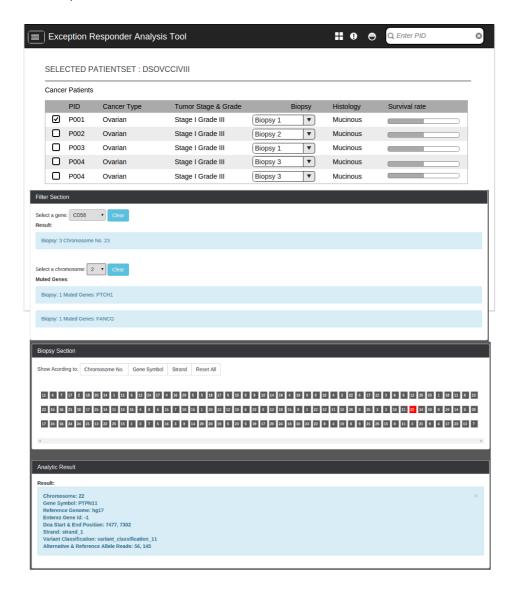
Results of "Make Patient Sets" are categorized according to their type, histology, stage and grade.



PD4. PATIENTS SETS INFORMATION

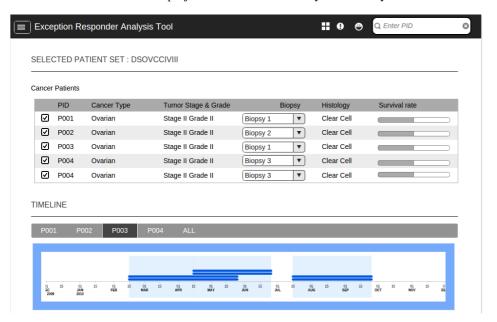
By clicking the "Magnifier icon" on the "Patient Set" would lead to the "Patient Sets Information" page. Here user can mine the data of the patient according to the biopsies, gene symbol, chromosomes and strand value.

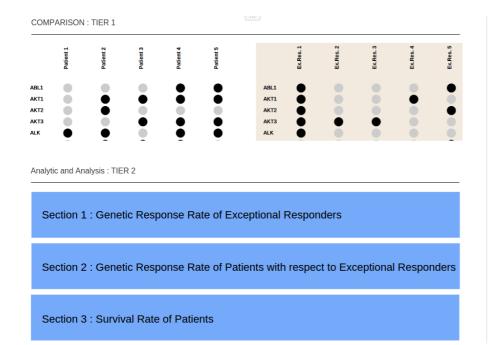
A prototype can be found here: http://ayusharma.in/exception-responder-proto/app/#/singlepatient



PD5. ERI HOME

This is the main section of the project and contains the analytic and analysis features.





Section 4: Similarity Rate between Patients and Exceptional Responders

Section 4.1: Similarity Rate between Patients and Exceptional Responders according to mutations

Section 4.2: Similarity Rate between Patients and Exceptional Responders according to genes

Mining Part: TIER 3

Section 1: Scatter Plots

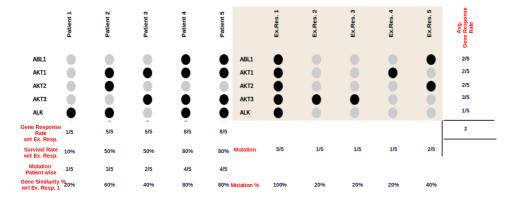
Section 2: Tree Layouts

Section 3: Advance Mining

TIER 1: VISUALIZATION

Calculation of Visualization Image

Note: Following image is consider for further calculations. I mentioned it as "Tier 1: Visualization Image"



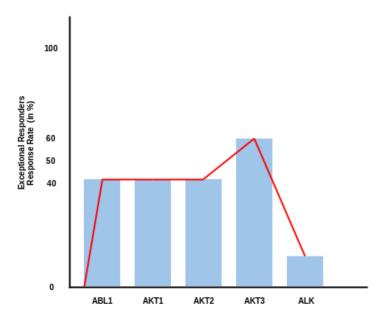
TIER 2 SECTION 1 : Genetic Response Rate of Exceptional Responders:

Average Response Rate of Exceptional Responders is calculated for every gene. In "Tier 1: visualization image" Ex. Resp. 1 & Ex. Resp. 5 (2 out of Five Ex. Resp.) are showing mutation in ABL1 gene show it's avg response would be 2/5.

Similarly for each gene the Average Response is calculated.

Let convert ABL1 gene Response to Percentage = (2/5)*100% = 40%

Similarly Average Response for every gene is calculated and following graph is plotted:



TIER 2 SECTION 2: Genetic Response Rate of Patients with respect to Exceptional Responders:

From t"Tier 1: visualization image" only ALK gene is mutated in Patient 1 and it's value is equal to 1/5. So Response Rate for Patient 1 = 1/5 Similarly we can calculate,

Response Rate for Patient 2 = (AKT1)+(AKT2)+(ALK)

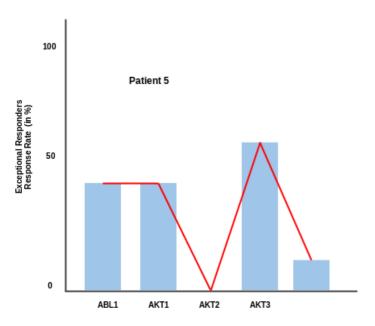
Patient Response Rate for Patient 2 = (2/5)+(2/5)+(1/5) = 5/5

Patient Response Rate for Patient 3 = (2/5) + (3/5) = 5/5

Patient Response Rate for Patient 4 = (2/5)+(2/5)+(3/5)+(1/5)=8/5

Patient Response Rate for Patient 5 = (2/5) + (2/5) + (3/5) + (1/5) = 8/5

Plotting Response Rate graph for Patient 5.



TIER 1 SECTION 3: Survival Rate of Patients

We can find the survival rate of the each patient if we compare the Gene Response Rate of every patient with Overall Average Gene Response Rate of Ex. Resp. (Which is 2).

So Survival Rate of Patient 1 = (Gene Response Rate of Patient 1/Overall Avg. Gene Response Rate of Ex. Responders)*100

$$= [(1/5)/2] * 100\%$$

= 10%

Similarly,

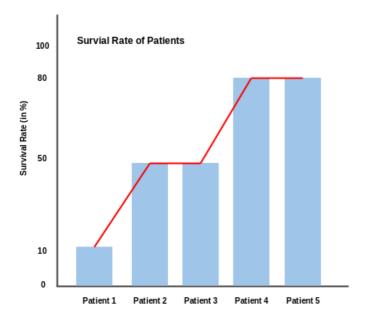
Survival Rate of Patient 2 = [(5/5)/2] *100 = 50%

Survival Rate of Patient 3 = [(5/5)/2] * 100 = 50%

Survival Rate of Patient $4 = [(8/5)/2)^*100 = 80\%$

Survival Rate of Patient 5 = [(8/5)/2] *100 = 80%

Drawing the Graphs of Survival Rates of Patients:



TIER 2 SECTION 4

Our next task is to find Similarity Rate between Patients and Exceptional Responders, which would cover the following objectives:

- 1. It will help to identify that which patient is similar to which exceptional responder.
- 2. It will help in analysis of drug and medicine over a period of treatment.
- 3. Comparison of every exceptional responder with every patient.

I illustrated Similarity Ratel in two sections

- 1. According to the no. of mutations occurred.
- 2. According to the gene percentage.

TIER 2 SECTION 4.1 According to the no.of mutations occurred

Average mutation of every Patient and Exceptional Responder = (Total number of mutated genes in a Patient & Exceptional Responder)/ Total number of genes

For Patient 1 = Total number of genes mutated / total number of genes = 1/5 = 20%

Similarly,

For Patient 2 = 3/5 = 60%

For Patient 3 = 2/5 = 40%

For Patient 4 = 4/5 = 80%

For Patient 5 = 4/5 = 80%

Similarly,

For Ex. Resp. 1 = 5/5 = 100%

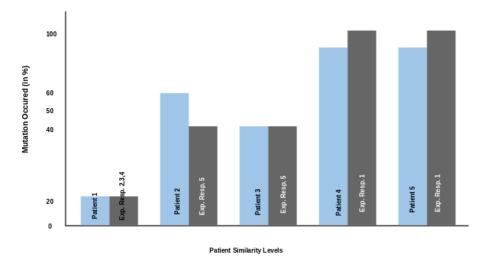
For Ex. Resp 2 = 1/5 = 20%

For Ex. Resp 3 = 1/5 = 20%

For Ex. Resp 4 = 1/5 = 20%

For Ex. Resp 5 = 2/5 = 40%

Drawing a plot for Similarity Rate according to the Mutation occurred:



TIER 2 SECTION 4.2 According to the Gene Similarity

In the Visualization Image we can see the that Patient 1 has only 1 gene (ABL1) similar to exceptional responder 1.

Patient 1 Gene Similarity Rate = 1/5*100 = 20%

Similarly For,

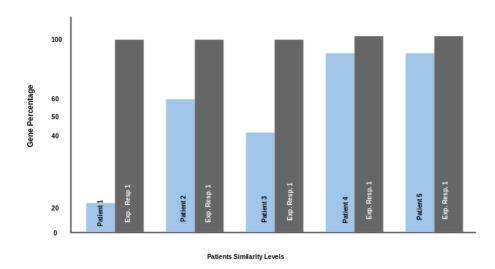
Patient 2 Gene Similarity Rate = $\frac{3}{5}$ *100 = 60%

Patient 3 Gene Similarity Rate = $\frac{2}{5}$ *100 = 40%

Patient 4 Gene Similarity Rate = \frac{4}{5} *100 = 80\%

Patient 5 Gene Similarity Rate = \square *100 = 80\%

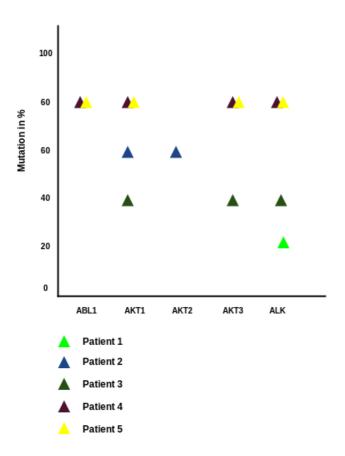
And we draw the plot as follows:



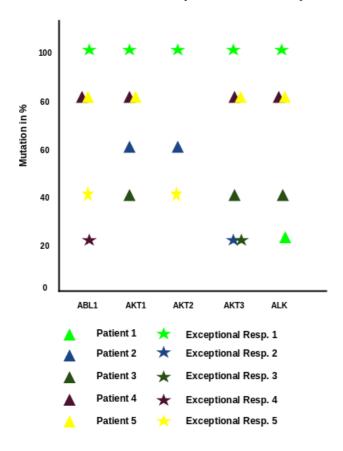
TIER 3 SECTION 1: Scatter Plots

I have drawn three sets of scatter plot according to the Mutation Percentage of the Patients and Exceptional Responders (Mutation % is mentioned in "Tier 1: Visualization image").

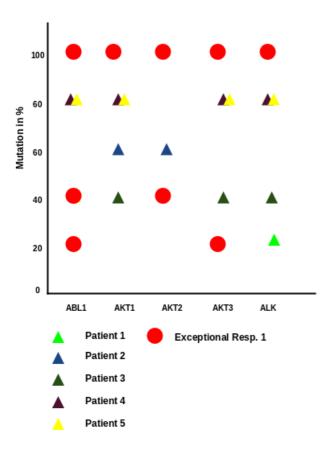
First Scatter Plot: In first scatter plot I only considered the patients:



Second Scatter Plot: In second scatter plot I considered Exceptional Responders and Patients.

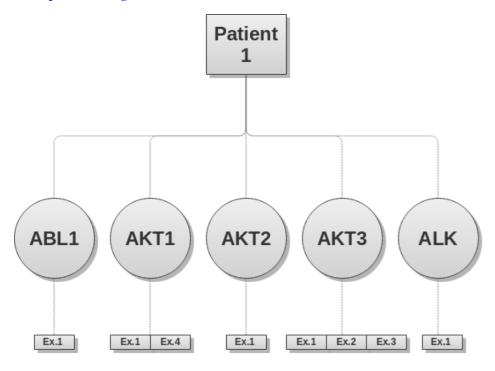


Third Scatter Plot: I have introduced exceptional responders as red mark to simplify the scatter plot.



TIER 3 SECTION 2: TREE LAYOUT

Information of specific Exceptional Responders as well as Patients can be represented in the tree layouts. Each patient will be the root node of it's gene and gene is connected to the Exceptional Responders. Tree would be flexible so the branches can be opened and closed. for ex. http://bl.ocks.org/robschmuecker/7880033.



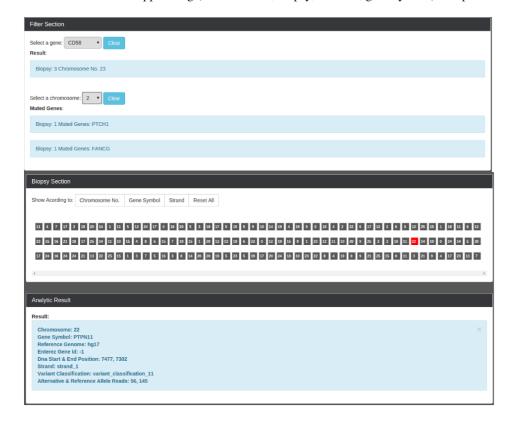
http://bl.ocks.org/robschmuecker/7880033

TIER 3 SECTION 3: ADVANCE MINING

This section would mine the data of the patient according to the prototype:

http://ayusharma.in/exception-responder-proto/app/#/singlepatient

Here filter can also be applied. eg (chromosome, biopsy, timeline, gene symbol) for specific results.

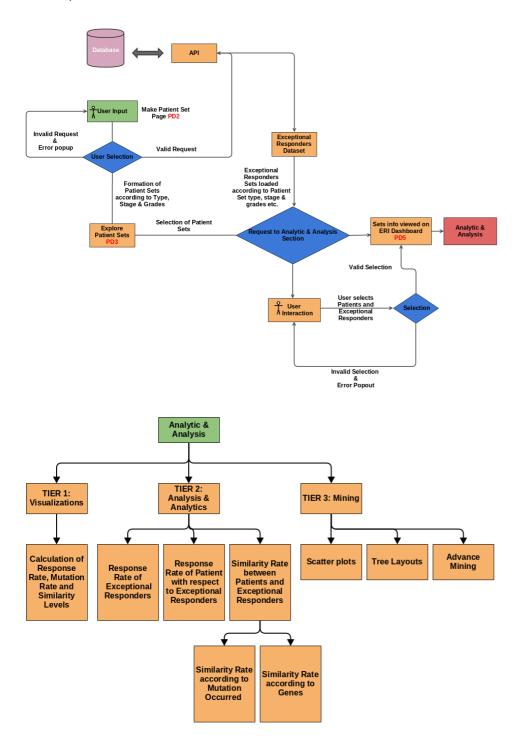


Each row of chromosome no. is represent the each Biopsy.

8. WORKFLOW

I have made the workflow of the whole system.

Blue Color: Initial Stage. Cherry Red: Final Stage



9. IMPLEMENTATION

Implementation of the project is divided into three paths:

- Basic Approach
- Technical Approach,
- Documentation & Communication
- Deliverable
- Future Aspects

Basic Approach

- Step 1. Case Study: Study and analysis of cancer along with factor which to be considered for the Exceptional Responder Analysis.
- Step 2. Resource Development: Discussion of idea, strategy and approach with mentor and get the solution of challenges and problems.
- Step 3. Technical Mock-ups: Modular approach is determined to code the whole idea and approach into reality.
- Step 4. Differentiation of Modules: Every strategy and idea is divided into modules and separately prototyped.
- Step 5. Integration of Prototype: All working modules will be integrated with each other in a single prototype.
- **Step 6. Testing & Issue:** Prototype is tested in different conditions, Feedback and Review is recorded, and all the work will be documented. This section has following objectives:
 - 1. Catch as many errors as possible.
 - 2. Track the error to understand their cause and any pattern that may exist.
 - 3. Re-Validate the stability of the solution.

Issue tracker is to be implemented on Github.

Technical Approach:

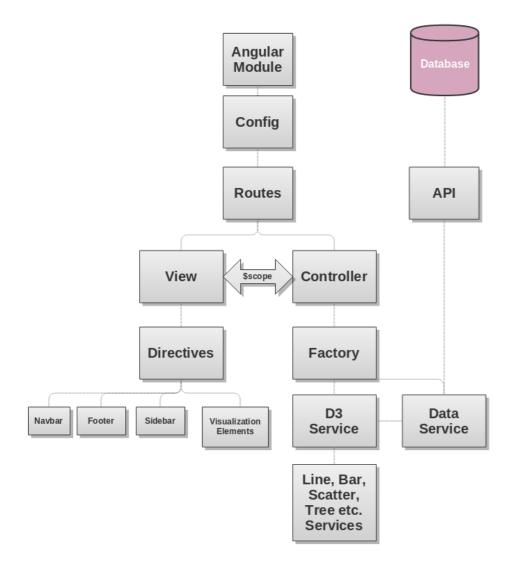
As mentioned on the project synopsis that Application should be written in Javascript. So I am going to use Angular JS, D3JS, HTML5, LESS and Ubuntu Machine.

HTML & LESS: These would be use for the markup and styling of the UI part. Less is a dynamic CSS which support functional parameters to css file.

Angular JS: It is a MVC platform which greatly support REST API and code is so optimized to understand. It also support modular approach very well as sections can be categorised into Directives , working would be handle by routes and controller, data and visualizations would be handled by factory.

D3JS: Most widely use framework around the globe for Analytic and Analysis visualizations.

Bootstrap: Bootstrap framework would be used for the UI and it would be in angularised format for better performance and code optimization.



Documentation & Communication

During the whole project every day report would be managed and given to mentor. Blogging and documentation part also done along this. It has the following objectives:

- 1. To sync the whole project with timeline.
- 2. check the direction of work and proper guidance from mentor.
- 3. identify the loopholes and progress rate of the project.
- 4. make everything easy, simple and understandable.

Deliverable

A Platform for exploration of Patient & Exceptional Responders sets to analyse the personalize care of normal patient and survival rate according to the genetic mutation of the exceptional responders.

Future Aspects

- 1. Sign IN & Sign Up criteria.
- 2. Profiling of the user/researcher, patient and exceptional responders.
- 3. Facility to import more visualization techniques.
- 4. Advance search and filtering of the datasets.
- 5. Addition of more visualization libraries like Highcharts and Grafana.

10. TIMELINE & ROAD MAP

Blogging, documentation and project report every day.

27 April to 24 May (Community Bonding Period)

- 1. Further discuss the idea and activity with mentor.
- 2. Study of cancer and it's analysis process.
- 3. Study of the requirement and analysis of the project
- 4. Creation of detailed wireframes.
- 5. Setting up the development environment.
- 6. Sharpen skills on Data visualizations methods, D3 JS and Angular JS.
- 7. To Understand the API Parameters, schema and constraint.
- 8. Discussion of documentation style with mentor.
- 9. I would love to code in sublime text editor.

25th May to 26th June (Working Period)

Week 1:

Start Coding.

Architecture

- 1. Construction of Exceptional Responder Analysis Tool architecture
- 2. Configuration of Angular Module for initial base with HTML/LESS.
- 3. Integration of API service (Data) with Visualization service(D3 JS).
- 4. Cross Origin Remote Source Validations and Configurations.
- 5. Testing to check the architecture of the system.
- 6. Wire frames layout would be coded into the UI for look and feel.

Formation of Patient Set

- 1. Implementation of Making Patient Sets Page.
- 2. Formation of Patient Sets using the API data.

Week 2:

Patient Set & Exceptional Responders Set Mining

- 1. Implementation of the Patient Set Data Mining along with Exceptional Responders Set mining.
- 2. Full information of each biopsy of Patient as well as exceptional responders according to biopsy, chromosomes and genetic symbols.
- 3. Data download facility would be added.
- 4. UI Enhancement of the system.

Week 3:

Patients and Exceptional Responders

- 1. Start to build the ERI Home Page, Patient Bar, TimeLine section and Visualization(TIER 1) for Mutated genes in patient.
- 2. TIER 1 analysis of Avg. Response Rate, Percentage Mutation, Survival Rate, Similarity Rate according to number of mutations and genes.

Week 4:

Preparation for Mid term Evaluation

- 1. Preparation for Midterm Evaluation.
- 2. Start coding for TIER 2.
- 3. Testing and Debugging of the completed work.
- 4. Issue resolving.

26 June to 3 July (Midterm Evaluation)

Deliverable:

- 1. Patient & Exceptional Responder set would be completed along with it's Mining Part.
- 2. ERI Home page would be coded and TIER 2 visualizations and calculation to some extent.

3 July to 18th August (High Work Period)

Week 1:

TIER 2

1. Completion of Coding of TIER 2.

Week 2:

TIER 3

1. Start Coding of TIER 3.

Week 3:

TIER 3

1. Completion of Coding of TIER 3

Week 4:

Binding UP the TIER Coding

- 1. Binding Up the TIER coding Tasks.
- 2. UI Enhancement.
- 3. Testing and Debugging.
- 4. Issue solving.

Week 5:

Code optimization

- 1. Pending issue and work would be completed.
- 2. Code optimization.

Week 6: Reserved for any unexpected delays.

18th August to 28 August (Pencil Down)

1. Testing & Documentation

11. ABOUT ME

AYUSH SHARMA

Country: India

IRC: ayushpix (Freenode)

Time zone: UTC+5:30

Email: ayush.aceit@gmail.com

Github: https://github.com/ayusharma

Web: http://ayusharma.in

Mode of Communication: Basecamp, Email, Hangout

Availability: 3 PM - 2 AM (IST) and 9:30 AM - 8:30 PM (UTC)

Targeted Time Per Week on Project: 50 hours approx.

Bioinformatics: I am not from Bioinformatics background.

Summer Interval: I have not proposed any activity for this summer.

Basic Information:

I am a **third year, computer science engineering major student at Arya college of Engineering & IT, Jaipur, India.** In my introductory and upper-level coursework, I've developed a passion for computer science and am extremely interested in contribution to Onco Blocks on the Project **Exceptional Responder Analysis Tool**.

I have worked on many technologies like HTML, CSS, LESS, JS, MVC, Python, C/C++, Git and Linux. I am also a Firefox student ambassador and contributor to the Mozilla Firefox community. My projects are as follows:

- 1. <u>Spiffout -An consumer Engagement System (Bootstrap, AngularJS, LESS)</u> (Internship): The Project is a web based consumer engagement platform which connects consumers to businesses and provides consumer satisfaction analytic.
- 2. <u>Blood Collective</u> (MIT Media Lab Design Innovation Workshop 2015): A community driven blood donation network application which gives the real time geo location of the blood donors.
- 3. <u>Kiwi An android application (AngularJS, Ionic and Apache Cordova)</u>: A Dictionary application for Android and Firefox OS, which provide definition, examples, pronunciation & much more of the input word. The app also includes activities like 'Word of the Day' and 'Match the column' to improve the vocabulary of the user.
- 4. <u>Medical Assistance System (HTML, CSS, JS, PHP, MySQL)</u>: The project is an undergraduate college project which gives the details of the doctors on the basis of symptoms.
- 5. <u>Pixelcount Creative Lab (HTML, CSS3, JS, MySQL, PHP)</u>: A personal project and self-startup to learn, deploy new technologies to get into web designing & Live Streaming. The project comprises a digital ocean droplet with responsive designed website, Databases, Mail server & GNU/Linux.
- 6. India- A Tribute (HTML, CSS, JS): A tribute to the martyrs of the freedom fighters of India.
- 7. Rajasthan Live: A live webcast website which comprises RTMP based live streaming, Provide NEWS about politics, sports and entertainment.

Contribution: I am a core team member (cloud) of Google Club, openmoz(Mozilla) and Mozilla Community Rajasthan.

I have also contributed to BioJs and PHPBB communities before announcement of the GSoC organizations.

https://github.com/biojs-edu/biojs-vis-snipspector/graphs/contributors

https://github.com/ayusharma/phpbb-website/graphs/contributors

https://github.com/ayusharma/website-assets/graphs/contributors

Apart from this I am a bright student of our college. I love photography and Nature. I have tried to make this proposal self explanatory but in case, any of the part is not clear in any form, I would love to be communicated. Feedback and suggestions are appreciated and would be helpful to keep me going. Thank you for your time and consideration.

0 comments

31/08/15 4:56 pm Review Proposal

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Version 2-1-20150730 (Report Bug)