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The Genomic Medicine Game

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Abstract. With advancements in genomics technology, health care has been improving and new paradigms of medicine such as genomic medicine have evolved. The education of clinicians, researchers and students to face the challenges posed by these new approaches, however, has been often lagging behind. From this the Genomic Medicine Game, an educational tool, was created for the purpose of conceptualizing the key components of Genomic Medicine. A number of phenotype-genotype associations were found through a literature review, which was used to be a base for the concepts the Genomic Medicine Game would focus on. Built in Java, the game was successfully tested with promising results.

Keywords. Genomic Medicine, Personalized Medicine, Genomics, Education, Pharmacogenomics, Gamification, Precision Medicine

1. Genomic Medicine

Since the establishment of the human genome project [1], biomedical researchers and clinicians have hoped that accessing individual genomic information would grant access to a whole new world of information that could be linked with different disease related aspects [2]. For more than a decade, genomics has been, without doubt, a hot topic in life and biomedical sciences due to its relevance in fundamental research, aiming to improve our understanding of the genomic variants that exist in our genome and how these variants can be associated with the causes and risks of suffering certain diseases and the molecular mechanisms of diseases. On the other hand genomics has been associated, since its early developments, with an enormous potential for translational science and the development of clinical applications in the areas of diagnosis, prognosis or therapeutics. These clinical applications have led to the development of what has been known as genomic or personalized medicine [3,4] and more recently precision medicine.

As it happens with other disciplines, the science and technology of the field are continuously evolving. In the case of genomic medicine, technological advancements have facilitated a drastic drop in the time and costs of sequencing from the 3 billion

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dollars and ten years of the original Human Genome Project, to the current massive parallel sequencing technologies that reduces the time of sequencing to a few days and the costs to a few thousand or even hundreds of dollars. These costs reductions have fostered the development of solutions and approaches at the diagnostics level and in therapeutics as companion diagnostics kits and therefore, personalized medicine. In parallel to these advancements, a different and new model has been designed with the development of direct-to-consumer (DTC) genomics. Companies have entered into genomics offering different options to capture and present genomic data to consumers, for different purposes such as genealogic studies and other health related applications such as pharmacogenetics [5] and associated risk for complex medical conditions [6]. For all these reasons there is an increasing pressure and demand of genomic related services associated with a higher demand from health professionals, researchers and even the general public to improve their understanding of the different sources of genomic variation and how they associate with different health-related aspects.

2. The Genomic Medicine Game

During the advance of genomic medicine, one of the most commonly mentioned obstacles is the lack of confidence of health professionals, other than those related with the field of genetics, to understand and interpret the results derived from genomic tests [7]. This need of training in the field is a recurrent topic in the analyses of the major gaps for the advancement and application of genomic medicine. Different approaches have been proposed in this area using approaches based in the analysis of real genomic data from students [8] or the use of cadaver sequencing [9]. These proposals benefit from granting access to the students to real data but present other drawbacks such as the cost of sequencing or ethics.

Our proposal, the Genomic Medicine Game (GMG), is an educational tool designed to support genomic education and help clinicians, researchers, students and potentially a broader sector of society to better understand the basis of genomic medicine by showing the basics of human genomic variation and their relationships with different health-related conditions. The genomic medicine game is supported by genome simulation followed by a role-playing game based interaction with the audience where each of the participants is given an individual genome with a different set of phenotypic and environmental factors so they can learn about their different interactions. Figure 1 shows the overall structure of the GMG.

3. Methods

3.1. Selection of genomic, phenotypic and environmental profiles

A key element for the development of the GMG is the development of a manually curated knowledge base with a selection of different environmental factors (such as smoking, sedentary lifestyle, diet and drug prescription), phenotypes (nicotine addiction, bleeding and different warfarin metabolism speeds or, Crohn's disease) and genomic variants (namely single nucleotide polymorphisms or SNPs, copy number variations or CNVs, and haplotypes), some of these relationships are shown in table 1.

The knowledge base contained information about the bibliographic references supporting the different environment-phenotype-genotype associations as well as the influence of the environmental factors. This knowledge base was then encoded in the application for its use in the generation of the genomes used in the role-playing activities.

Table 1. This table shows of some of the relationships between genomic variants, environmental factors and phenotypes used in the knowledge base applied for the development of the GMG.

Environmental factor	Genomic variant involved	Phenotype
Smoking	SNP	Nicotine addiction
Diet, smoking, sedentary life style	SNP	Coronary heart disease
Drug prescription (Warfarin)	Haplotypes	Increased risk of Bleeding
Diet, Smoking, intestinal Infection	CNVs	Crohn's Disease

3.2. Implementing the genome, phenome and environmental factors profiles

The GMG case generator module is responsible for the generation of the profiles that are going to be used during the role-playing activity. We chose Java as the development platform with the aim of facilitating the widespread use of the GMG. The GMG has a graphical user interface designed to be simple and easy to use. This interface allows the activity coordinator to select the different environmental variables that are going to be used during the simulation. The graphical interface also allows the selection of the types of genomic variants of interest, in case the game is used to illustrate just a certain kind of variation. Once the user has defined the relevant variables for the generation of the profiles and genomes to be used during the game, the system is then able to generate the profile files. The system also includes the use of Bayesian networks to infer the probabilities of presenting a certain phenotype (disease) given the specific profiles generated.

The final output is a set of ".pdf" files containing the profiles that are going to be handed to the participants in the simulation. Each of these files contains a 1:1,000,000 scale individual diploid genome containing all chromosomes represented at the referred scale and different variants according to their allelic frequencies, and three tables containing, a summary with the variants included in the genome, the environmental factors and finally the phenotypic traits according to the parameters previously defined and the results from the Bayesian inference process.

4. Results

4.1. The Genomic Medicine Game case generator module

The GMG module was tested on different OS platforms (Mac, Windows, Linux) to ensure its use across them. This testing process validated its simple interface, its capability to generate large numbers of simulated genomes and the correct use of the allelic frequencies among the simulated genomes.

Individual genomes and phenotypic/environmental profiles were generated as ".pdf" files that could be printed and handed to the participants for the role-playing simulation stage of the game. In these, the genomes variants are located in their proportional location within the chromosomes and are colored to facilitate their

location, in this regard and to facilitate their location the system provides a table with their coordinates.

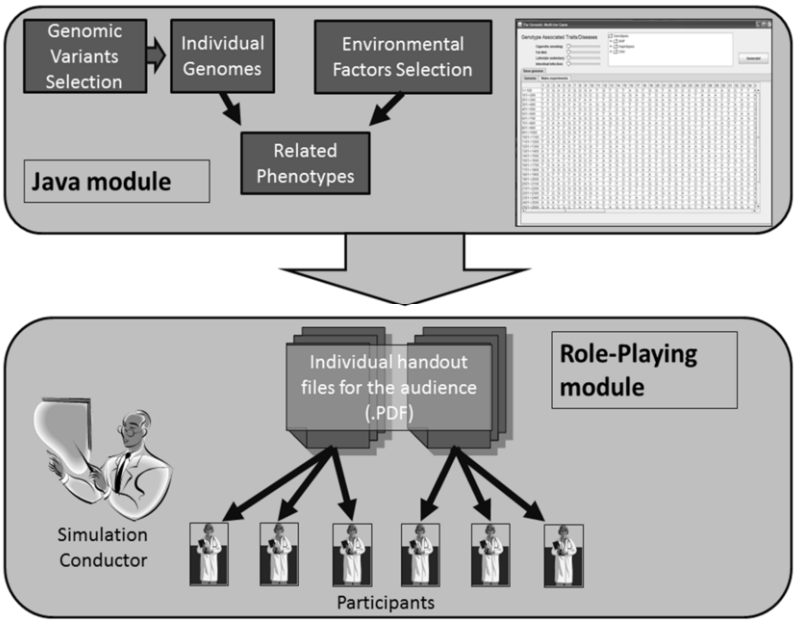

Figure 1. The Genomic Medicine Game is divided in two modules. The Java module enables the selection of parameters and simulation of the genomes whereas the second module involves the role-playing element with the participants

4.2. Using and testing the Genomic Medicine Game

The dynamics of the game involves handling the participants with their own generated genomes and then asking them questions that showed the different association between phenotypic traits, environmental factors and genotypes. We ran a successful initial demonstration of the Genomic Medicine Game with a group of health professionals with different specialties andackgrounds (n=24). The dynamics of this demonstration included an initial explanation of the aims and purpose of the experience, followed by the role-playing experience were all the different variants were explained using the three different scenarios included.

After completing the game we asked the participants to fill a small survey to rate their experience and express their feelings and suggestions for the future. The quantitative results of this small survey are presented in table 2. With a mean range of 4.3 to 4.6 and a median range of 4 to 5, where 5 is totally agree and 1 is totally disagree, this indicates the capabilities of the GMG and the potential it has in the field of genomic medicine. Interestingly the results showed the utility of the GMG as an educational tool for both students (question 3) and health professionals (question 4). The slightest lower mean in question 4 is due to a higher dispersion in the responses (StDev 0.6 vs. 0.8) most likely due to the different background (specialty) of the participant. This diversity would explain as well the lower median value in question 5.

Table 2. Summary of results the initial test of the genomic game. 24 professionals were involved in the cohort, and saw potential in the Genomic Medicine Game. Answers were rated in a 1 to 5 scale meaning 1 totally disagree and 5 totally agree.

Question	Mean	Median	Min	Max
1. I think the game is useful for understanding concepts about genomic medicine.	4.4	5	3	5
2. The game dynamics were easy to follow.	4.5	5	3	5
3. I think students would find the game as a useful educational tool.	4.6	5	3	5
4. I think health professionals would find the game as a useful educational tool.	4.4	5	3	5
5. I think the examples selected are interesting and relevant.	4.3	4	3	5

5. Conclusions

The Genomic Medicine Game is a tool for teaching the fundamental elements for genomic medicine, combining audience engagement, genome simulation and the use of a curated knowledge base. The GMG offers an alternative to other educational approaches involving real data or static examples by mean of the dynamic generation of simulated genomes. In addition the GMG shows the complexity of health application of genomics due to the interaction genome-environment-phenotype making explicit use of those relationships in its examples.

We have tested the GMG with a group of health researchers with promising results. Participants engaged in the role-playing dynamics, and suggested as future improvement an expansion of the current number of examples included in the exercise. For this reason we plan a new version that will be web-based therefore improving accessibility and will contain an improved and extended knowledge base with new concepts and scenarios aiming to help conceptualize Precision Medicine.

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