Gap Analysis of Scientific Research on RARE DISEASES IN THE ARAB WORLD.

Facts and Figures

Rare diseases are defined according to their prevalence, and it is generally accepted that disorders affecting less than 5 persons in 10,000 of the general population are classified as *rare diseases*. It is estimated that 1 out of 17 persons suffer a rare disease, this amounts to 7% of the population. Many argue that classifying these diseases as *rare* falsely implies a considerable deal of insignificance; however according to the aforementioned percentage, the Arab world is predicted to have approximately 25 million sufferers from rare diseases. The list of known rare diseases currently includes around 8000 entries and with new rare diseases being described every month by researchers, the list is certainly getting bigger.

From a patient's perspective, rare conditions are often chronic and life-threatening. There is, however, a great deal of heterogeneity among rare disease in terms of prevalence, clinical progression and etiology. For some conditions, prevalence rates in certain countries are relatively high to an extent that referring to them as "rare" is not technically correct. On the other end of the spectrum, there are conditions affecting very few individuals (or even a single person) in a whole country. The significance of prevalence rates from patients' viewpoint is that the degree of medical and social support, they are likely to get, can be directly linked to the presence of others who suffer from the same condition. It is often the case that research on rare disorders is instigated by pressure groups formed around patients and their families, and the queue of diseases to be investigated in depth by medical science is very long indeed. This report highlights the status of research on rare diseases in the Arab world in order to identify current shortages and avenues for improvement.

Box 1: The Arab Council of Geneticists: The Centre for Arab Genomic Studies (CAGS) in Dubai developed a network of Arab clinical geneticists and molecular biologists from all over the Arab World (the Arab Council). These efforts are in line with the general strategy of the Centre to help accelerate the process of uncovering the molecular mechanisms of genetic disorders in order to alleviate human suffering through optimized treatment and/or preemptively combat disorders through proper diagnostics. Moreover, through its comprehensive genetic database for Arab populations (see **Box 2**); CAGS offers the chance to obtain a complete view of all the aspects relating to genetic disorders in Arab countries. Through the CTGA database, it is possible to compare and contrast genetic research and genetic data from various Arab countries. Thus, CTGA allows proper interpretation of information from this part of the world and facilitates viewing

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The Clinical – Molecular Gap in Research

It is very important to remember that the vast majority of rare diseases have a considerable genetic component to their causality. However, geneticists are seldom the first port of call for patients and families that suffer from these conditions.

Since 75% of rare diseases affect children, it is hardly surprising that practicing doctors (pediatricians in particular) are the ones who come first into contact with affecteds. The process of recognizing previously identified conditions or reporting novel ones starts with a detailed description of the clinical features including laboratory findings. However, it is usually the case that the genetic underpinnings of the disorder have to be uncovered in order to understand its pathology and come up with effective diagnostic tools and potential therapeutics.

To this end, there is a tremendous need worldwide to bridge the vast gap between medical practitioners and researching molecular biologists.

Clinical geneticists provide a link between the clinic and the research lab; however these professionals are very few and far between. As a matter of fact, Arab countries suffer severe shortage in both clinical geneticists and academic courses that train local students in this field of science.

Box 2: Catalogue of Transmission Genetics in Arabs (CTGA): The first step towards tackling the burden of rare diseases in the community goes through proper characterization of the current picture of these disorders on the local and regional levels. The Centre for Arab Genomic Studies (CAGS) carries out this complex task for all genetic disorders in Arab populations. Both clinical and molecular data are collected by CAGS after being reviewed meticulously. CAGS ensures high quality of its input data through the internationally recognized process of scientific peer-reviewing. Collected data is analyzed and organized to be fed into the Centre's Catalogue of Transmission Genetics in Arabs database (also known as CTGA). The latter has developed qualitatively and quantitatively over the past few years to become the largest ethnic-based database worldwide. Screening CTGA for Rare Diseases in the UAE and other GCC countries yields a great wealth of information that can provide proper guidance for healthcare providers and policymakers.

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Research on Rare Diseases in the Arab World; Gulf Cooperation Council Countries as an Example.

The CTGA database has been accumulating data from peer-reviewed studies on rare diseases and other genetic disorders in the Arab world for over a decade now. On querying CTGA on rare genetic disorders and by analyzing the actual content of these studies; it is possible to obtain precise information about the collective characteristics of research performed on rare diseases in this part of the world.

Key characteristics of research on rare diseases in UAE, Oman, Qatar, Kuwait, Bahrain and Saudi Arabia are depicted in **Figure 1**, which clearly shows the shortage of studies that choose to go beyond clinical description of symptoms to investigate deeper causality. For Oman, Qatar, Kuwait and Bahrain only 10 – 14% of studies included molecular investigations of the genetic causes of rare disorders. Fortunately, the numbers are much better for UAE and Saudi Arabia, even though there is plenty of room for improvement. It must be mentioned, however, that this abundance of "clinical-only" studies is not restricted to GCC countries or to the subject of rare genetic disorders. Only 33% of the total entries in the CTGA are genetic ones, while the rest are phenotypic studies as shown in **Figure 2**.

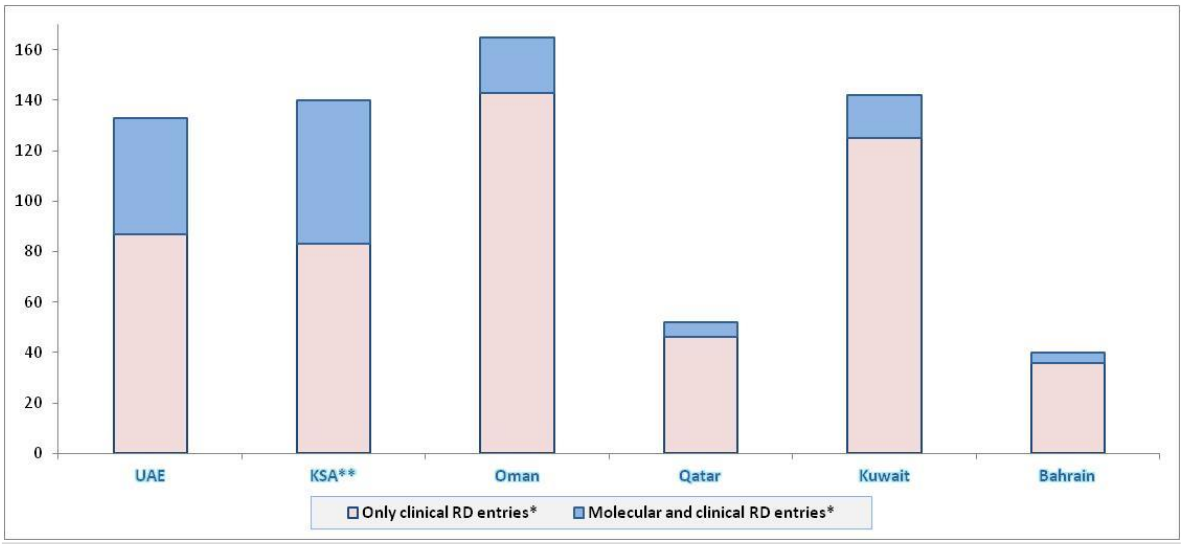

Figure 1; numbers of molecular versus non-molecular entries for rare diseases in Gulf Cooperation Council countries according to the CTGA database **(last updated 3 Feb 2015).**

* Phenotypic entries in CTGA with prevalence rates <10/100000 live births.

** Data from UAE, Oman, Bahrain, Kuwait and Qatar is up to date, while KSA data is being updated at the time of writing this report.

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Ethnocentricity of Global Genetic Research

Information on mutations in genes for the purposes of both research and constructing guidance for clinical decisions has been the focus of scientists worldwide. Industrialized nations have been more successful in developing country/ethnic-specific mutation detection, archiving and prevention strategies. However, from the beginning of epidemiological screening it was clear that genetic variants follow distinct profiles in different ethnicities/populations; this transpired upon researching diseases such as thalassemia and phenylketonuria (PKU). The latter fact highlights the need for specific screening of genetic variants in various populations, and undermines the assumptions that data obtained in certain populations automatically apply to others. This was the main driving force behind establishing the CTGA database that revolves around genetic data gleaned from various Arab populations. Building up an "Arab" genetic database is even more relevant when considering the subject of rare diseases, because studying local cases of these disorders, which might be unknown elsewhere in the world, is regarded as a responsibility of the local researchers in the first place.

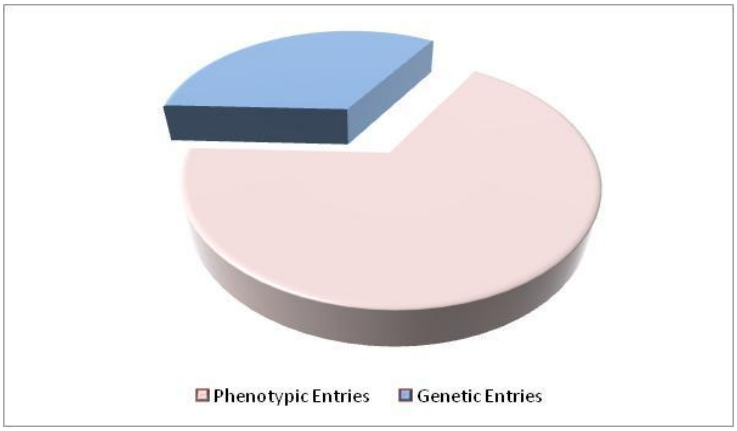

Figure 2; A graph representing the full content of the CTGA database reaching 1860 entries classified under "genes" or "phenotypes" **(last updated 3 Feb 2015).**

Conclusions

Genetic research in the Arab World has been focusing mainly on clinical studies and skipping the more difficult – but essential – genetic investigatory work. Many Arab countries have high levels of consanguinity and, consequently, of recessive genetic disorders, and therefore the need is immense to mobilize resources towards more molecular research. This will allow for the development of ethnically-specific diagnostics and therapeutics that achieve superior results in terms of prevention and treatment. Additionally, it is high time more attention and resources were given to the training and education of future clinical geneticists in the Arab world. Current numbers of these specialists is alarmingly low in all Arab countries and this problem has to be addressed before any improvement can be achieved in healthcare provision.