### SHORT COMMUNICATION

## IVF empowered by NGS: redefining reproductive medicine through PGT-A and PGT-M

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#### Introduction

Medicine has always strived to cure disease. However, 11

when it comes to genetic disorders, the truth is sobering: 12

95% of these conditions remain without a cure, and only 13

a handful, perhaps 5%, benefit from licensed therapies 14

(1). For families at risk, this means facing heartbreaking 15

16 choices, limited options, and lifelong burdens. But what

if the best way to address these disorders is not to treat 17

them at all, but to prevent them from arising in the first 18

place? 19

This is precisely what Preimplantation Genetic Testing 2.0

2.1 (PGT) has made possible. By examining embryos before

implantation during in vitro fertilization (IVF), PGT 22

empowers couples and clinicians to make decisions 23

that were unthinkable a generation ago. With PGT for 24

Aneuploidy (PGT-A), embryos with chromosomal 2.5

26 abnormalities can be identified, sparing families the

anguish of miscarriage or the birth of a child with severe 2.7

chromosomal syndromes (2). With PGT for Monogenic 28

Disorders (PGT-M), embryos carrying single-gene 29

diseases, such as sickle cell disease, can be avoided 30

31 altogether (3).

At the Molecular Genomics and Precision Medicine 32

Department, ExpressMed Diagnostics and Research, 33

Bahrain, we have witnessed this transformation firsthand. 34

To date, we have conducted nearly 700 PGT-A cases and

25 PGT-M cases, the majority of the latter for families 36

affected by sickle cell disease, a significant health burden 37

in our region. 38

Our own analysis has highlighted the striking impact of 39

maternal age on chromosomal abnormalities. Among 40

women aged 25-30 years, the incidence of embryo 41

42 aneuploidy was already as high as 60%. Alarmingly,

43 in women over 40 years, this figure rose to nearly

90%. These findings reinforce a truth long known in 44

reproductive medicine: advancing maternal age is the 45

single most important factor driving chromosomal errors,

failed implantation, and miscarriage. PGT-A therefore 47

provides a powerful safeguard for older women seeking

to conceive, improving the likelihood of selecting a viable embryo.

The advantages are compelling. PGT-A improves implantation rates, reduces pregnancy loss, and accelerates the path to a successful live birth. PGT-M prevents the inheritance of specific genetic diseases, breaking the cycle of transmission within families. These are not abstract outcomes, they are life-changing realities.

The technology itself has advanced remarkably. With Next-Generation Sequencing, we can now analyze embryos with extraordinary accuracy, detecting chromosomal errors and pinpointing single-gene mutations in a single workflow (4). This highly sophisticated platform enables high-throughput, cost-effective, and precise results, making PGT an indispensable tool in modern precision reproductive medicine.

However, it is important to recognize that PGT is not without challenges. The high cost of testing and IVF procedures can limit access for many couples, particularly in low-resource settings. Furthermore, biological complexities such as embryonic mosaicism—where both normal and abnormal cells coexist in the same embryo can complicate diagnosis and interpretation, occasionally leading to uncertain outcomes. Addressing these limitations through better counseling, standardization, and cost optimization remains a crucial goal for the field.

Another important dimension of PGT is the ability to determine the genetic sex of embryos. While this must always be approached with strict ethical safeguards,

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it is essential in cases of sex-linked disorders such as
 hemophilia or Duchenne muscular dystrophy (5). Here,
 choosing the "right" gender is not a preference but a
 prevention.

The implications for public health are profound. In regions like the Middle East, where consanguinity and genetic disorders remain common, PGT offers a preventive strategy at the earliest possible stage, before life begins (6). Instead of managing untreatable disorders across a lifetime, we now have the opportunity to stop them from being passed on at all.

#### Importance of PGT-A in the GCC and Bahrain

The Gulf Cooperation Council (GCC) countries, including Bahrain, face unique genetic health challenges 91 due to high rates of consanguineous marriages and 92 the prevalence of hereditary conditions such as sickle 93 cell disease, thalassemia, and metabolic disorders. In 94 Bahrain, for example, sickle cell disease continues to 95 be one of the most common inherited disorders, placing 96 significant social and healthcare burdens on families 97 98 and the medical system. PGT-A and PGT-M provide a direct means to address these challenges by reducing 99 miscarriage rates, preventing the birth of affected 100 children, and lowering the long-term healthcare costs 101 associated with chronic genetic disease. Importantly, 102 103 these technologies also offer hope to couples who might otherwise feel they have no safe reproductive options. As 104 awareness and accessibility increase, PGT could become 105 a cornerstone of reproductive health strategies in the GCC, complementing existing newborn screening and 107 108 premarital testing programs.

#### **Conclusions and Future Perspectives**

PGT-A and PGT-M represent a paradigm shift in reproductive medicine, moving the focus from treatment to prevention. By enabling couples to avoid the transmission of genetic disorders and reducing the emotional and physical toll of failed pregnancies, PGT offers a vision of healthier families and healthier societies.

Nonetheless, for this promise to be fully realized, the field must confront key limitations such as cost, accessibility, and biological uncertainty. Continued innovation and collaboration will be necessary to make these technologies universally available and ethically

122 sustainable.

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Emerging adjunct technologies are poised to further 123 transform this landscape. Artificial intelligence is 124 increasingly being integrated into embryo selection 125 and genetic data interpretation, enhancing accuracy and 126 reducing human bias. Non-invasive embryo testing, 127 analyzing Deoxyribonucleic Acid from spent culture 128 media rather than embryo biopsy, may 1 day minimize 129 risks to embryo integrity. Additionally, advanced 130 imaging and time-lapse systems now allow for real-time 131 assessment of embryo development, complementing 132 genetic insights to improve selection outcomes.

Looking ahead, the future of PGT lies in broader accessibility, integration with personalized medicine, and continued advances in genomic technologies. Cost reduction, streamlined laboratory workflows, and greater awareness will be essential for ensuring equity of access. Ethical oversight will remain critical, particularly as technology expands into areas such as polygenic risk scoring and expanded carrier screening.

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For Bahrain and the GCC, embracing PGT as part of a comprehensive public health strategy against genetic disease could dramatically reduce the prevalence of inherited disorders in future generations. By prioritizing prevention before birth, we can ensure that the promise of precision medicine is realized where it matters most: at the very beginning of life.

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#### **List of Abbreviations** 155 Artificial intelligence 156 GCC **Gulf Cooperation Council** 157 **IVF** In vitro fertilization 158 NGS Next generation sequencing 159 PGT-A Preimplantation Genetic Testing for Aneuploidy 160 PGT-M Preimplantation Genetic Testing for Monogenic 161 Disorder 162

#### **Conflict of interest**

The authors of this article have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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