

Gold Nanoparticle Based High Throughput Screening

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Abstract. In the COVID-19 pandemic that began in January 2019, antigen detection has made an immeasurable contribution to the pre-detection of the virus. Conjugates with gold nanoparticles (Au NPs) are distinguished. At the same time, nucleic acid detection is widely used in the accurate detection of a large number of samples, and it is a high-throughput detection method. HTS technology is a feature of future and present bio-detecting, which can make targets more easily and accurately detected, while Au NPs could be gained without too much cost and help build high throughput characterization, as well as enabling pre-detection. Thus, the combination of both HTS technology and Au NPs are widely expected and researched for their future potential. This article reviews the detection method combined with gold nanoparticles and high-throughput technology, which makes the detection more efficient, can carry a larger sample base, and has a high degree of accuracy. By researching on building HTS and making use of Au NPs, the detecting technology can be fully improved and can help fasten the progress being made in pharmaceutical industry, thus creating a promising method for preventing epidemic.

Keywords: High throughput characterization, gold nanoparticles, antigen detection.

1. Introduction

High throughput screening (HTS) is a type of characterization used in the field of biopolymer detection. By decorating the surface of certain targets with HTS technology, detection can become more efficient and accurate. What is more, HTS technology can save lots of costs and provide better results, thus start taking the place of traditional methods of detection since being developed. Gold nanoparticles are usually a part of the HTS technology, for their specific feature of combining biomolecules while not changing the own characteristic of them, by which they could be decorated in various ways and create different detection methods to achieve high accuracy and efficiency, also serving as an important visual detection method to classify the existence of targets.

High-throughput characterization first originated in 1984 and was implemented in Nagoya, Japan. It is an efficient screening of natural products with various fermentation conditions [1]. Natural products screening, having multiple fermentation conditions, is implicitly high throughput [1]. Researchers believe that this high-throughput screening method can increase the screening speed to 10,000 samples per week, and increase the screening capacity by 50 to 100 times [1]. Its most common working principle is to perform special treatment on the surface of the substance to be tested or combine it with special receptors, etc., and detect it through specific instruments. In the following three decades, high-throughput technology has gradually gained greater importance in the field of biomedicine, and technology giants have obtained dozens of patent certificates for HTS technology. The technology of high-throughput characterization mainly focuses on the detection or screening of substances to be tested. The HTS program is used to isolate high-yield microbial cell factories is an example of the current application of HTS technology [2]. The detection technology for high-throughput characterization has now become quite mature, and it has played a significant role in the fight against the new coronavirus.

Compared with traditional detection methods, HTS has significant advantages, including: (i) more efficient detection mode and extensive application of automation, which not only reduces labor costs and detection error probability, but also effectively improves the carrying capacity of detection technology, such as microplate and flow cytometer (FACS) to establish automated operating system and culture analysis mode (ii) HTS technology is highly sensitive and can detect corresponding results in a very short time; iii) The number of samples required fewer,. For example, when using microplate

detection, the necessary sample quantity is only a few milliliters, and when using liquid droplets for detection, the required sample quantity is even only in the nanoliter level. By reducing the number of samples, the time and cost of cultivating the samples to be tested can be significantly saved [2]. With the vigorous development and the global epidemic of the new crown epidemic, medical testing based on a large number of samples is particularly important, and to ensure a certain detection rate, high-throughput testing methods have gradually become indispensable. Au NPs based HTS.

2. Au NPs Based HTS

Over the past few years, advances have been made in cell testing technology and instrumentation [3]. Which consists of HTS-compatible technology to measure G-protein-coupled receptor (GPCR) and ion channel function, confocal imaging platforms for fast cell and sub-cell imaging, and the ongoing development of reporter gene technology [3-5]. At the same time, gold nanoparticles have been used to label macromolecules since their discovery, and in biochemistry are mostly used to label proteins, which is known as one of the four modern labelling methods. Gold nanoparticle has been to be utilized for visual analysis due to its high molar absorption ratio [6-10]. Au NP-based colorimetric method utilizes minimum lab instrument and is promising to be applied in point-of-care testing (POCT) [1].

As for Au NPs, they become different colors at different sizes, and seed growth is usually used to obtain these particles, mainly adding thiol ligands to control their size. Due to their high electron density, each gold-labeled protein appears black individually and turns red when aggregated, allowing these aggregates to be easily seen for effective visual pre-detection. At the same time, through the high binding affinity of gold nanoparticles and specific biopolymer fragments, it can play a discriminative role in the high-throughput detection process to ensure the specificity and accuracy of detection; at this time, gold nanoparticles can become ligands and receptors. The intermediate substance between the ligands ensures the binding relationship between the ligand and the polymer fragment to be detected, and at the same time plays a pre-detection role. Therefore, in high-throughput characterization and detection, it often plays the role of labeling specific substances and grafting other labeled substances to achieve high-precision and high-specificity detection. For example, the decoration of the DNA probes on the surface of the Au NPs via covalent interactions between AU and S can be used for DNA colourimetric detection, as well as miRNA or small molecules [3]. Overall, Au NPs have advantages such as fast and easy synthesis, narrow size distribution, effective surface change by thiols or other bioligands, and desirable bio-compatibility, thus are used in HTS technology [11].

For the detection of proteins, gold nanoparticles are indispensable indicators. Although it is usually only used for preliminary visual detection, it has considerable high-throughput detection characteristics, which can detect a large number of people at the same time, while ensuring the accuracy of detection to a certain extent. For proteins, labeling with gold nanoparticles is only a modification of the protein surface and will not change its properties, which also makes gold nanoparticles a common way of use as an intermediate for binding or interacting with proteins such as fluorescent groups. At the same time, the resonance characteristics of Au NPs have also been commonly applied in the detection of proteins, that is, gold nanoparticles produce different colors in different volumes due to the resonance effect with incident light, which is of great significance in qualitative and semi-quantitative detection [12]. At the same time, the covalent compound of gold nanoparticles and silver also has certain detection characteristics. When using gold nanoparticles, the binding of receptors to proteins is often a major point, because gold nanoparticles often have high attraction to life macromolecules due to their high charge density. Just like the binding of an enzyme to a specific receptor, it is necessary to adapt the receptor by changing the shape and size on the surface of the protein so that it can bind spontaneously. Gold nanoparticles mainly play the role of assisting connection, and can also perform visual pre-inspection, which is an excellent collaborator of high-throughput technology.

3. Research Progress

In today's biomedical applications, fluorescence—whether radio-fluorescence, fluorescence carried by cellular and subcellular proteins, or fluorescence emitted by fluorophores—is the primary phenomenon used to detect proteins of interest in order to construct high-throughput characterizations. Measuring fluorescence with a fluorometer can help identify the presence or absence and specific concentration of a target protein, resulting in an efficient, orderly, and high-throughput assay. The fluorescence method based on gold nanoparticles will not interfere with normal visual detection, and the measurement of fluorescence can be automatically measured by special instruments, which can accurately determine the concentration of protein solution and whether it is damaged or mutated while being efficient.

When using fluorescent probes to detect specific proteins, peptides are usually used to construct probes, and then fluorescent modification groups are labeled on the peptide probes. Due to the difference in the modification method and type of the polypeptide, it has affinity and specificity for different types of proteins, so it can avoid the target from binding or interacting with other proteins or other substances to produce fluorescence, so as to achieve the purpose of detecting the target protein. Usually, in order to achieve high-throughput detection, the method of dual fluorescent modification groups is adopted, using a fluorescent quenching group and a fluorescent emitting group respectively. Probe reporter groups fluoresce when peptides bind or interact with proteins to cause structural changes. Using special instruments to monitor the fluorescent signal, the presence and concentration of substances such as proteins or nucleic acids of interest can be measured.

Another method for establishing high-throughput characterization is the radiation method, which requires the use of radiolabeled amino acids. Au NPs are labeled with amino acids. When Au NPs are combined with proteins, the labeled amino acids will decompose and emit fluorescence. By detecting the presence and intensity of fluorescence, the presence or absence and concentration of the target protein in the solution can be judged. Fluorescence analyzer. The fluorescence intensity and properties produced by radioactivity are different from those produced by the fluorescent probe method, so the detection instruments and achievable precision are also different (actually, with improved detection equipment, the detection and stability of the radiation method are better). In this method, gold nanoparticles are not only used as an intermediate substance between the labeled amino acid and the target protein, but also as an identification agent for the target protein, which produces a specific effect. However, the radiation method has hidden dangers and will cause harm to human safety, so the demand for testing sites is high, which also makes it difficult for radiation methods to be replaced in small and medium-sized enterprises.

The latest state-of-the-art detection method is the detection of specific cells. After the most common treatment of adding ssDNA, gold nanoparticles are added and mixed with the test sample. Through the laser imaging system, the source of visible light and the fluorescence of the cell itself can be clearly determined, and even the internal structure of the cell can be directly imaged. Although this method is sufficiently efficient and capable of high-throughput characterization, it is still not a substitute for radiation-based methods and fluorescent probes for protein detection. The reason is because of the high cost of the instrument. This state-of-the-art method has high accuracy, high stability, and considerable speed compared to the other two more traditional detection methods, but unfortunately, this detection method is not only costly, but also often requires biochip technology, which means that it is technically demanding, so it has not been widely used. The other two traditional detection methods are efficient and accurate. Although it is lacking compared with the latest technology, it has also made an immeasurable contribution to the current epidemic prevention and control.

Of course, not using fluorescence related methods, Au NP based high throughput screening still has other methods. For example, antibodies conjugated to gold coupled with silver valorization were used in histochemistry and later in dot and blot assay [13]. By combining immunoglobulin G in the human body with biotin-conjugated anti-IgGs, and then washing with double distilled water. After adding gold nanoparticles and silver enhancement solution, the gold nanoparticles will form a colloid

at the position where IgG is fixed because of its binding properties with biomacromolecules. A large amount of precipitation [13]. This method is remarkable because the spots formed by the silver deposits are very easy to see, so some commercial cameras can be used for discrimination. In addition, the tone and gray scale of silver deposition depend on the number of gold nanoparticles, so the concentration of the substance to be tested can be judged by measuring these two indicators [13]. Although this kind of method could be only applied to a few kinds of virus, it still provide a way with low instrumental cost, high accuracy and easy operation steps, while it can be easily detected visually, thus make the feature of gold nanoparticles more useful in the whole method.

In addition, gold nanoparticles based on technologies such as temperature conduction can also be used in high-throughput technologies, and have been applied as emerging technologies in some fields, such as LAMP technology.

4. Conclusion

In this review, a detection technique that makes use of HTS and Au NPs has been introduced. Specifically, the mechanism and recent research progress have been presented. This technique can increase detection efficiency, carry more samples, and improve accuracy. To sum up, gold nanoparticle based high throughput characterization technology, which is still an innovation, are widely used in pharmaceutical industry, clinical and biomonitoring, and have promising future use to help develop these fields. In addition, this kind of technology has helped a lot in the context of the Covid-19 pandemic, and is ready for usage in epidemic prevention.

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