Human Hair as a Testing Substrate in the Era of Precision Medicine: Potential Role of 'Omics-Based Approaches

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Abstract

Minimally and noninvasive investigation of pathology and treatment monitoring is highly attractive in medicine. The use of human hair samples as a non-invasive testing substrate is potentially poised to improve diagnostic and forensic medicine. Hair has the unique ability to capture long-term information about health and disease in an individual as compared to urine and blood. Testing long hair offers a potential means of long-term monitoring of drug compliance, drug abuse, chronic alcohol abuse, and diagnostic biomarker discovery. Even though human hair is mostly composed of keratin and keratin-associated proteins, very little literature has been published on human hair proteomics. Emerging high throughput omics based techniques such as proteomics are increasingly improving our depth of knowledge about the diagnosis, prognosis and prediction of diseases globally. Although many aspects of the use of these novel molecular aids to improve disease diagnosis and patient management remains elusive; it is evident that these techniques have improved precision medicine tremendously. This chapter aims to discuss current plausible application of human hair omics-based approaches to the field of pathology, diagnostics and precision/individualized medicine.

Keywords: human hair, proteomics, precision medicine, hair testing, diagnosis, forensics

1. Brief history and background of human hair testing

The history of hair analysis dates back to as far as the nineteenth century. Precisely in 1858, Hoppe published a report on the discovery of arsenic in the hair of a human corpse exhumed

after 11 years [1, 2]. Almost a decade later, amphetamine was discovered in the fur of a guinea pig by Goldblum et al., in 1954 [3]. In the late 1970s, Baumgartner et al., developed what is now known as a radioimmunoassay (RIA) kit for the detection of opiates in hair [4]. Thus, laying the groundwork for the first contemporary use of hair in drug testing. This method which was first introduced to Germany by Arnold in 1980 generated a lot of controversies [5]. However, subsequent work by Klug [6] that same year provided a basis for the use of hair in forensic toxicology by confirming the RIA method with thin-layer chromatography and fluorescence detection. Also, the inception of gas chromatography with mass spectroscopy (i.e. GC/MS) 6 years later, led to improved detection, sensitivity and specificity at low cost. Therefore, increasing the number of newly discovered compounds [1]. Over the next three decades, advances in chromatographic and spectrometric techniques coupled with new methods of sample preparation and wash procedures have enhanced the detection limits from ng/mg range to pg/mg [7]. Microscopic hair analysis, as another tool for hair testing, only began to gain a rapid recognition in the early twentieth century. For instance, the books published by Glaister in 1931 on the study of hairs and wools on mammals [8], and that of Hick on the microscopy of hairs in 1971 [9] both became a widely used resource for the forensic scientist in the use of hair as evidence in a crime scene. Preliminary findings from hair testing led to the American scandal of false imprisonment from evidence based on hair microscopy [10], which lead to severe scepticism on the validity of hair testing for analytical or forensic purposes.

Nonetheless, the scientific use of hair analyses and testing as a tool for forensic toxicology and medicolegal purposes, in the era of precision medicine, has proved valuable. More so, the recent need for a non-invasive method/testing substrates for early diagnosis and profiling of diseases based on their biology and molecular phenotypes [11], has made hair testing an attractive option. Also, application of non-invasive strategies improves patient compliance. Considering that the human hair is mostly composed of proteins; it is an attractive proteomic substrate for diagnostic and forensic pathology. Not least, the presence of other biomolecules (such as lipids) in hair indicates that an integrated multi-omics approach would significantly improve the field of investigative medicine [12].

It has been hypothesized that irrespective of ethnicity or hair form, there is biochemical and growth rate similarities in all hair types [13]. However, emerging evidence seems to suggest that differences exist in hair structure and growth rates depending on ethnic profile or grooming [14]. Human hair distribution and growth is androgen-dependent resulting in differences between males and females as well as regional variation within the same individual [15].

The human hair follicle contains stem cells in their bulge region and in the dermal papilla [16]. These stem cells are responsible for the significant self-renewal capabilities of the human hair follicle and the hair cycle. There are remarkable disparities in molecular structure and biology of human hair based on individual differences, gender, age, various hair grooming habits; chemotherapy/radiation exposure; cosmetics as well as diseases [17].

Omics-based techniques employ a holistic interrogation of the full complement of a biomolecule in a systems biology oriented manner. Although, many omics-based methods are yet to be employed routinely in hair testing and biomarker identification; there is reasonable hope that they will provide much needed insight to the biology and pathology of several medical conditions. This review intends to evaluate the current hair testing applications and potential benefits of hair omics-based approaches in diagnostic medicine.

2. Basic structure and biochemistry of the human hair

Human hair is a long, thin cylinder of keratinized cells that grows from large cavities or sacs called follicles. Hair is usually composed of three distinct regions: an inner cortex, an external cuticle and occasionally a central inconsistent medulla or core running along a central axis of thicker terminal hairs [18]. The cortex is primarily responsible for the mechano-physical properties of the hair fiber and is composed of long filaments called microfibrils which contain organized α-helical rods of keratin, embedded in an amorphous matrix [19] (**Figure 1**). Human hair is composed of 65–95% proteins, 15–35% water and 1–9% lipids, 0.1–5% pigments
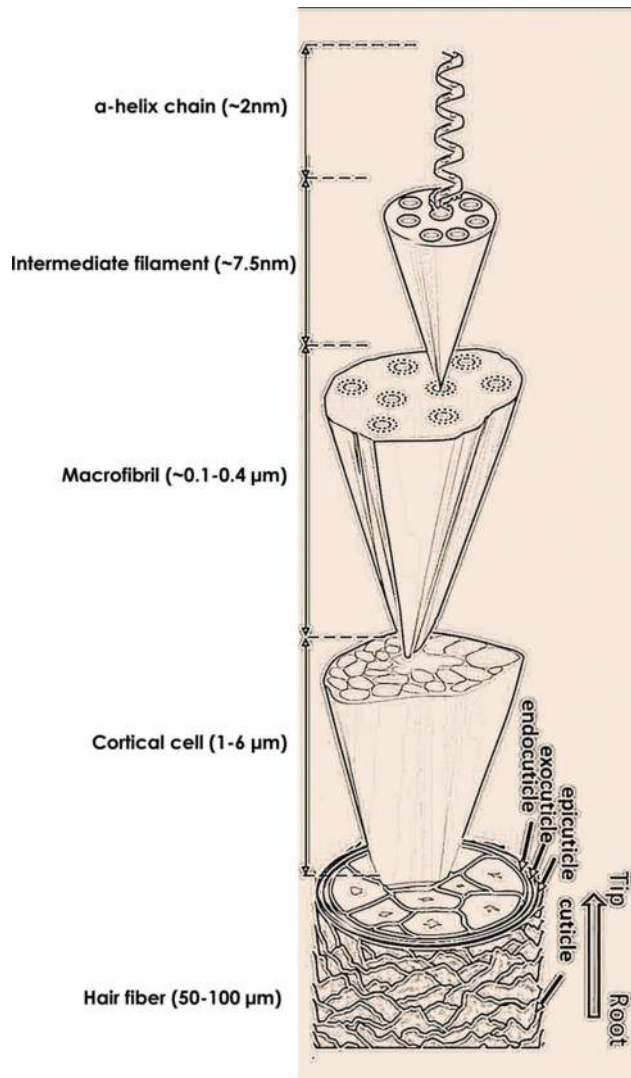

Figure 1. Complex structure of the human hair fiber (picture adapted with kind permission [128]).

(melanin), small amounts of trace elements, and polysaccharides [18]. Older studies suggest there is no significant difference in the amino acid composition of hairs from different racial group [20]; however, there is evidence that there are significant differences in the lipid composition of hair [21]. The hair fiber is rich in lipids either derived from sebum or secreted from the apocrine gland which consists of free fatty acids, mono-di-and triglycerides, wax esters, hydrocarbons, and alcohols [22].

On average, human scalp hair is reported to grow approximate 1 cm/month. However, recent data reports lower growth rates for hair originating from people of African ancestry. The human hair growth cycle consists of four phases called anagen (growth), catagen (transition), telogen (rest) and exogen (shedding phase) [23, 24]. During the anagen phase, the capillary blood supply around the follicle provides nutrients and delivers any extraneous materials that may be present in the blood stream such as drugs or toxins [10]. Although the mechanism of the incorporation of drugs or metabolites into hair is not clear, three pathways have been proposed and are generally accepted by scientists including: active or passive diffusion of drugs into the bloodstream feeding the dermal papilla, diffusion from sweat or other excretions the growing or mature fiber is exposed to and, external diffusion from vapors or powders into the mature hair fiber [25]. However, the relative importance of each pathway has not been elucidated and it is probable that the incorporation of drugs into hair may involve a complex series of events which may conceivably vary between different individuals.

3. Reliability of hair testing in precision medicine

In comparison with blood sample collection, hair collection is easy and non-invasive. It does not require any specialized equipment or storage facilities. It permits long-term storage at room temperature without any risk of contaminating the environment. There is reasonable evidence that using hair as a testing substrate in medicine is of tremendous benefit and that there are many unexplored possibilities to the use of hair testing in the evidence-based era of precision medicine. However, it is important to comment about the reliability of hair testing as this has far reaching ramifications in various scenarios. In a study that assessed the reliability of inter-laboratory and intra-laboratory variations in hair minerals using three different laboratories, a consistent numerical result was generated from all three laboratories [26]. However, the results were interpreted differently because each laboratory used different normal reference ranges. This indicates that variation in reported concentrations of specific analytes in hair would result in different interpretation of the patient's health status in each instance. Therefore, effective ancillary use of hair in diagnostic medicine requires standardization of normal reference ranges. Over- or under-reporting may be another factor that might affect the reliability of the use of hair as an alternative biological testing matrix. For instance, Vignali et al., found discrepancies between self-reported use and biological testing of illicit drugs use among inmates [27]. The authors explained that theses discrepancies might be due to false declaration of drug use in hope of qualifying for entry into rehabilitation programs. Also, illicit drug users with moderate risk may use levels below the limit of detection because
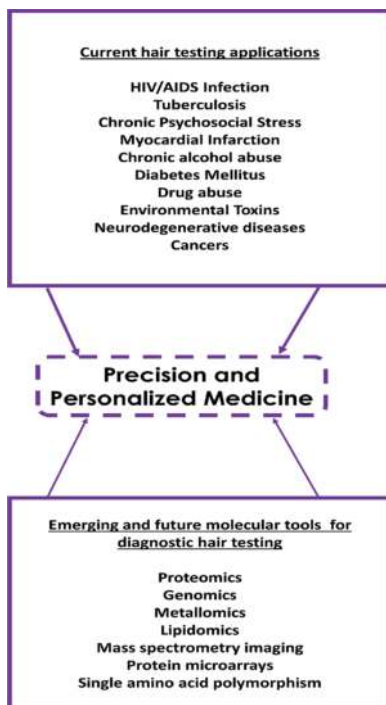
Figure 2. List of current application of hair testing in personalized medicine and future diagnostic potential of omics-based approaches for precision medicine.

there is inadequate empirical evidence of standardized minimum detectable levels of specific substances of abuse; hence, a negative test does not connote "no exposure" [28]. On the other hand, hair testing has become so reliable that it was considered better than urine, blood or breath testing, for demonstrating long-term illicit drug abstinence prior to solid organ transplant [29]. Hair testing may present a complementary test in scenarios where the veracity of conventional test results is in doubt. A summary of current and future application of hair testing in precision medicine is represented in **Figure 2**.

4. Current hair testing applications in medicine

The human hair is capable of long term incorporation of various exo- and endogenous compounds as compared with blood plasma or urine [30]. Changes in the physicochemical properties of hair as well as genetic, environmental and hormonal factors may result in various hair disorders [31]. Hence, a good understanding of the biology and the potential use of hair as a testing substrate in medicine is a very attractive option. Hair testing approaches have been applied for drug and biomarker monitoring in forensic and toxicological screening purposes as described below:

HIV/AIDS infection: Inadequate exposure to medication results in antiretroviral therapy failure, but unfortunately there are no robust methods for long-term monitoring of drug compliance in HIV/AIDS patients. Hair-based monitoring of protease inhibitors (like atazanavir and lopinavir) concentration have been reliably shown to be independently and strongly associated with treatment response [32]. Another study carried out by Hickey et al., demonstrated a relationship between nevirapine concentration and virological outcomes, although high levels of nevirapine found in women and older adults in their cohort require further research [33]. However, non-significant negative association between nevirapine and drug compliance has also been reported in a HIV-infected pediatric cohort [34].

Tuberculosis: Blood plasma monitoring of tuberculosis (TB) can be fraught with a lot of inconsistencies due to the relatively shorter half-life of the anti-TB drug in plasma as compared with hair. For example, low plasma levels of rifampicin, isoniazid, and pyrazinamide have been demonstrated in many pulmonary TB patients, despite compliance with the direct observation of treatment (DOT) strategy [35]. Inter-patient pharmacokinetics has made a reproducible assessment of drug compliance difficult in TB patients. More recently, adherence to anti-TB drug regimen has been monitored effectively in latent and active TB patients using a liquid chromatography coupled tandem mass spectrometry (LC-MS/MS) analysis to identify isoniazid levels in human hair samples [36]. Also, isoniazid levels have been monitored in pediatric population of TB patients using small quantities of their hair samples [37]. A landmark non-invasive multi-drug quantitative assay has also been developed, for measurement of multiple second line anti-TB drugs (moxifloxacin, pyrazinamide, linezolid, and levofloxacin) in multi-drug resistant types of TB, using hair sample testing [36].

Chronic psychosocial stress: Chronic stress has a detrimental impact on human health if allowed to persist indefinitely. An important physiological response to stress is the stimulation of the hypothalamic-pituitary-adrenal axis and release of cortisol [38]. Due to diurnal variation in cortisol release, measurement of cortisol levels in body fluids such as urine, blood and saliva may be fraught with inconsistencies [38]. Hence, hair cortisol level measurement is now being used as a surrogate biomarker for chronic psychosocial stress [38, 39].

Myocardial infarction: Acute myocardial infarction (MI) can be precipitated by acute stress, albeit the role of chronic stress in acute MI is poorly understood. Human hair testing is emerging a reliable method to measure cortisol levels around episodes of acute MI. An enzyme immunoassay-based approach has been used to demonstrate higher cortisol levels in the most proximal 3 cm portion of the hair of acute MI patients as compared to patients without acute MI [40].

Chronic alcohol abuse: Beside its use to detect alcohol consumption and monitor abstinence from alcoholic beverages, ethyl glucuronide a stable metabolite of ethanol has the capability for long term monitoring of alcohol abuse using hair samples. Whilst other tests such as breathalyzer, urine test, and blood test are capable of short term records of ethyl glucuronide (at most 3–4 days), hair is capable keeping track of months of alcohol abuse. The efficacy of hair testing for ethyl glucuronide as a biomarker of chronic alcohol abuse is well established [41].

Diabetes mellitus: Diabetes mellitus (DM) is a leading cause of morbidity and mortality globally; with global estimate of people with DM projected at 300 million by the year 2025 [42].

Long term damage, failure, and dysfunction of various body organs can result from the chronic hyperglycemia that characterizes DM [43]. Westernization of diet as well as lifestyle has been suggested to be a contributory factor to the development of DM in Africa [44]. As far back as 1960s and 1970s, researchers have investigated in various cohorts, the correlation between the level of chromium in human hair and DM [45]. Later on, hair protein glycation has also been used for long-term DM treatment monitoring. For example, glycated products such as furosine has been correlate fairly with the yearly mean values for HbA1c and fasting plasma glucose in a study by Oimomi et al. [46]. Also, a spectrophotometric hair glycation index has also been shown to be reliable to differentiate between normoglycemic and hyperglycemic individuals [47]. More recently, determination of derivatized amino acids in human scalp hair using gas chromatography-coupled mass spectrometry, revealed differential molecular signatures between DM patients and controls in a Jordanian cohort [48]. Thus, analysis of human hair is a promising approach to long-term evaluation of DM and other diseases.

Drug abuse: Hair testing is a key area of growing interest in the fields of forensic sciences because it can be sampled without difficulty from human subjects. Also, hair possesses the ability to store chronological record of drug use and abuse. Human hair testing has led to accurate measurement of levels of various illicit drugs such as amphetamines, cocaine, cannabis, opiates, phencyclidine, barbiturates and methamphetamine have been measured using radioimmunoassay and gas chromatography coupled mass spectrometry [49].

Assessment of exposure to environmental toxins: Environmental exposure to various toxins may accumulate and lead to various health problems. Normally, exposure to xenobiotic agents induces post-translational modifications (PTMs) to proteins [50], they may induce heat shock proteins [51] and lead to the induction of phase-I and phase-II detoxification enzymes [52]. Currently, exposure to environmental toxins (such as heavy metals, insecticides, polycyclic aromatic hydrocarbons (PAHs), endocrine disruptor pesticides, etc.) can be evaluated by the use of hair testing [53–57]. Although promising, hair testing for environmental toxin may be fraught with inaccuracies due to factors such as the lack of analytic validation methods, low interlaboratory reliability and the poor delineation between endogenous toxicants and exogenous contaminants in hair [58].

Neurodegenerative diseases (ND): Hair testing is gradually finding a role in molecular assessment of NDs [59]. For example, differential PTMs of proteins are manifested in response to ND. Two NDs, Menke's kinky hair syndrome and Elejalde disease are characterized by hair changes that may be of great diagnostic value [60]. Both conditions result in irreversible brain damage and early death and hair abnormalities seen in these patients help to differentiate these conditions from other NDs [60]. Scalp hair trace element content has been used to diagnose multiple sclerosis [61]. Also, red hair phenotypes have been associated with greater risk for Parkinson's disease [62]. Further molecular studies are needed to explore noninvasive diagnostic in the field of neurodegenerative medicine.

Cancers: As in the case with ND, differential PTMs and expression of proteins are manifested in response to cancer. Also differential expression of various trace elements in hair have been found for different types of cancer, in a study carried out among Polish [63] and Indian [64] populations. X-ray diffraction of hair, used in combination with mammography

has been reported to significantly improve the sensitivity and diagnostic accuracy for invasive Breast Cancer [65]. A meta-analysis demonstrated that hair zinc levels in female breast cancer patients were lower than those found in controls, albeit this difference could not be picked up in serum [66]. Cancer-associated hair phospholipids can also be potentially used for development of a reliable screening hair-based test for breast cancer [67].

5. Future perspectives

5.1. Experimental Omics-based molecular hair testing

Various omics-based approaches have allowed researchers to interrogate the full complement of molecules in complex biological systems. Up to 73 species of ceramide lipids have been identified using shotgun lipidomics analysis [68, 69]. Also, there is a positive correlation between hair arsenic, sodium and iodine levels and risk of cancer development in a metallomic study [70].

Proteomic techniques have also been successfully utilized in hair [71–75]. Mass spectrometry based approaches have led to the identification of peptide biomarkers of oxidative chemical damage in hair, as well as to differentiate structural damage caused by cosmetic treatment/weathering hair diseases like monilethrix [76]. Also, mass spectrometry has been used to identify 343 proteins as natural constituents of the human hair [73]. Using liquid chromatography-coupled mass spectrometry-based shotgun proteomics, ethnic-based differential proteomics signature have been identified in hair keratin protein levels [75].

Also, mass spectrometry imaging (MSI) has become a major tool for tissue biomarker discovery [77]; as well as other applications such as tissue profiling in histopathology and drug distribution in forensic medicine [78]. Waki et al., utilized MSI technology to determine biomarkers for aging in the human hair cortex [79]. MSI has been shown to be able to monitor cocaine in a single strand of hair sample for forensic purposes [80]. The concentrations of cocaine varied along the shaft of the hair strand, which correspond to the chronological time the drug was ingested.

A protein microarray proteomics study identified autoimmunity related biomarkers for scalp lesions in alopecia areata [81]. This study identified eight potential antigen biomarkers specific for alopecia areata which were used for the design of a discriminant miniarray for alopecia areata and other scalp lesion [81]. Not least, single amino acid polymorphism (SAP) or non-synonymous single nucleotide polymorphisms (SNPs) are emerging as a potential approach for reliable human identification for forensic purposes [71, 82].

An important feature of all omics-based methods is their high dependence on data repositories, algorithms and bioinformatics workflows [83]. A "public data driven" approach for integration, mining, and reuse of data would benefit the field of omics immensely [84]. Although there are individual merits for each omics based field, an integrative multi-omics method may permit a more robust molecular analysis [85]. Despite the few available papers that have addressed the use of omics-based methods in the field of dermatology [86, 87], there still remains a dearth of papers that address the application of proteomics to human hair samples for non-invasive testing of various clinical conditions for precision medicine.

Hair metabolomics: The term metabolome refers to all the metabolites in a biological organism, with metabolites being the products of enzyme-catalyzed reactions that result from gene expression, protein synthesis and environmental stressors [88]. Metabolomics is a relatively new and dynamic field [89] and involves the study of "the complete set of metabolites/low-molecular-weight intermediates, which are context dependent, varying according to the physiological, developmental or pathological state of the cell, tissue, organ or organism" [90]. Depending on the length of the hair, endogenous compounds and physiological influences can be observed in hair over extended periods of time. Utilizing hair metabolomics in personalized medicine allows clinicians to deliver optimum care to patients [91]. Advances in this field enable the accurate determination of possible pharmaceutic toxicity, appropriate dosages and an individual's susceptibility to possible disease. In addition to physiological influences, co-metabolic factors are considered when investigating hair metabolomics [129]. This enables the examination of drug metabolism during the different stages of disease. Metabolomics is increasing used to understand and predict drug response in patients. For example, a gas chromatography-time of flight (GC-TOF) based platform was used to investigate the biochemical differences associated with the racial response to atenolol, an anti- hypertensive drug [92]. Other fields of study often are unable to account for various day-to-day factors present in individual lives. Combining hair metabolomics with other disciplines and rapidly advancing analytical methods enables a holistic investigation into metabolism and drug metabolism. An example of this is the identification of biomarkers for spontaneous preterm birth using hair metabolomics in conjunction with blood biomarkers [93].

Hair lipidomics: Lipidomics is a branch of metabolomics focused on the complete analysis of lipid species and their biological roles in health and disease. Lipids are analyzed using mass spectrometry (MS), chromatography and spectroscopy-based methods. Hair lipids are distributed throughout the hair fiber, they are hydrophobic, oily or greasy organic substances that are extractable from cells and tissues by nonpolar solvents, mainly chloroform and/or ether [94]. Lipids are designated as exogenous and endogenous depending on whether they emanate from sebaceous glands or hair matrix cells, respectively. Endogenous lipids, biosynthesized in the hair matrix cells accounts for approximately 2.5% of the entire hair fiber include cholesterol, sulphate, sterols and ceramides while exogenous lipids accounts for below 1% which include squalene and sterols [94] and is vital for maintaining the internal water content in the hair fiber [95].The application of lipidomics hair research is still in its infancy. MALDI-MS Redox lipidomics has been used to investigate lipid damage in human hair [96]. Studies showing the importance of lipids in in diseases such as alopecia [97], breast cancer [98, 99], and diabetes is sure to promote research in hair lipidomics.

5.2. Potential ancillary molecular tools for hair testing

5.2.1. Molecular imaging

Molecular imaging (MI) can be defined simply as the characterization and measurement of biological processes at the tissue; cellular and molecular level using optical techniques. In contrast to the 'traditional' diagnostic imaging, MI investigates the molecular abnormalities underlying a disease instead of the mere visualization of the end effects of the molecular aberrations [100]. Although the use of imagining in hair analysis is not new, the recent advancements have shown that the use of microscopy goes beyond the comparison and

identification of microscopic characteristics in hair. More so, the combination of microscopy with spectroscopy techniques promises to be a valuable tool for the molecular characterization of hair [101, 102]. Molecular imaging of hair in comparison to other biological materials is very useful particularly in diagnosis as it provides a useful testing or screening material with minimal invasion to the subjects. Examples of imaging tools used in the analysis of hair apart from mass spectroscopy imaging include the following:

Multiphoton fluorescence lifetime imaging (MFLIM): MFLIM microscopy is a method set up for the optical examination of biological samples [103, 104]. Due to the inherent sectioning capability of this technique, 3D images with subcellular resolution can be obtained as well as two-photon excited auto-fluorescence of endogenous fluorophores. In 2007, Ehlers et al., studied the bleaching effects, intrahair dye accumulation and other hair pigmentation properties of the human hair using a time-resolved MFLIM single photon counting and near-infrared femtosecond laser pulse excitation [105]. Two photon imaging have also been employed in the live imaging of stem cells and the study of progeny cells in hair follicle regeneration [106].

Synchrotron radiation X-ray fluorescence imaging (SRX): The use of synchrotron-radiation-excited X-ray fluorescence to analyze biological samples provides information about the presence of trace metals [107]. The minimal radiation damage of SRX imaging to specimens in comparison to other techniques involving the use of ion or electron probes makes this method a preferred choice to study the distribution of elements in pathological condition and pharmaceutical intervention [108]. The application of SRX imaging to study the dynamics of mercury in rat hair [107] and mapping of other trace elements in human using a muprobe have been reported [109].

Fourier transform infrared (FTIR) imaging: FTIR imaging has an advantage over other imaging techniques in that it is label-free, nondestructive and has a broad range of biomedical application [110]. Most especially, the use of the FTIR imaging in the attenuated total reflection (ATR) mode [111]. A key advantage of the use of ATR-FTIR imaging is that there is minimal sample preparation before analysis and the depth of penetration of infra-red (IR) light in the specimen is well controlled and is independent of sample thickness. Thus, allowing for a good spatial resolution of the imaged samples and even faster image acquisition (two to three orders of magnitude) when combined with array detectors such as focal plane arrays (FPA) or linear arrays [110]. Significant improvement in the signal to noise ratio have been recorded with the use of synchrotron as source infrared radiation. However, the use of this method is only suitable for very small specimen areas and will involve a mapping approach for the imaging of larger sample area. In addition, the spatial resolution obtainable with synchrotron radiation source in FTIR imaging is not desirable. However, the advent of Globar infrared source has improved spatial resolution and allow for a high detection and distribution of the chemical composition of biological samples [112]. Thus, the application of FTIR-ATR imaging has been used to obtain clear chemical images of the cross-section of the human hair and thus obtain information from the medulla without the problem of passive contamination of the adjoining cortex [113]. The different forms of FTIR and other examples of molecular imaging techniques mostly involving a combination of IR or non-IR spectroscopy techniques that have been used in hair analysis and diagnosis of disease with hair as substrate includes FTIR spectral micro-imaging [114, 115] infrared and Raman spectroscopy [116], Atomic force infrared spectroscopy (AFM-IR) [117, 118] and electron microscopy [119–121].

5.2.2. Nanotechnology/Nanomedicine

Nanotechnology involves the control of matter at the atomic or molecular levels, i.e. at the nanoscale (1–1000 nm). Hence, nanotechnology can be defined as methods or techniques employed in the processing of materials at the atomic or sub-atomic scale to generate products with physical and chemical properties that are different to the traditional counterparts [122, 123]. Nanomedicine, on the other hand, is the application of nanotechnology in medicine or health care. Recently, it has become possible to create nanoparticles that can function in an organized manner as biological sensors for the early detection, monitoring and treatment/management of diseases [122]. Nanomedicine has provided novel ways of diagnosis and treatment of dermatological conditions. Although much of the new technologies involving the coupling of nanotechnology with other testing methods are still under investigation, it is a known fact that nanotechnology promises to generate tools and devices that would lead to an increase in the accuracy of detection and analysis of biological samples (e.g. hair). Even though, the use of nanotechnology in trichology is not prevalent, most of the current and non-invasive methods of diagnosis involving the use of nanotechnology may apply to the molecular and structural analysis of hair. Such method that mainly includes imaging and chemical analysis are often referred to as "Nanoimaging" or "Nanoanalytics" [124]. Nanoimaging, which involve the use of nanoparticles to improve the optical and spatial resolution of test materials have proved very useful in diagnosis and testing. For instance, different nanoparticles have been tested in various diagnostic applications due to some advantages such as high sensitivity and specificity, which allow for the use of a little amount biological sample [124–126].

5.2.3. Monitoring trends of/compliance to a nutritional and/or physical activity (PA) protocol

Hair testing can potentially contribute to weight and physical activity monitoring. Exploring this approach would provide a more measurable and objective means to assess an individual's compliance to a reduced calorie, low carb and/or low fat dietary regimens. This is more reliable than what food frequency or PA questionnaires can accurately assess [127]. Post-translationally modified proteins, phase-I/-II enzymes, heat shock proteins, redox status proteins, etc. would be differentially expressed and may better capture dietary/PA compliance than what the classical clinical biochemical parameters (triglycerides, cholesterol, free sugar levels, etc.) would be able to do. These biochemical parameters are rather transitory and are prone to day-to-day confounding factors. For example, specific proteins may serve as excellent surrogate markers of steady-state homeostasis achieved by a more consistent compliance to a dietary or PA regimen.

6. Conclusion

We have discussed various application of non-invasive hair testing in the era of precision medicine and factors that have militated against the routine use of hair testing in diagnostic pathology. Establishing a workflow that can permit the routine use of hair as a testing substrate for disease diagnosis would greatly benefit diagnostic and therapeutic aspects of precision medicine. The use of emerging omics'-based molecular approaches in hair testing would shed more light on hair-based molecular signatures for various physiological and pathological conditions.

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Conflict of interest

The Authors declare that they have no conflict of financial or non-financial interest.

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