# Translating Epi-Proteomic Developments into Business Value for the Insurance Industry

Christoph Lüdemann and Moritz Völker-Albert

#### **Abstract**

Epigenetic and proteomic processes control central biological mechanisms and can be dynamically modulated by environmental and lifestyle factors. Epi-proteomics - the interplay of epigenetic modifications and proteomic changes - opens up new perspectives for preventive approaches in health management and for innovative applications in the insurance industry. Environmental factors such as diet, physical activity and chronic stress have been shown to influence epi-proteomic patterns, leading to long-term biological imprints that can be expressed, for example, in the form of a "epigenetic memory" of muscle or fat cells. These molecular signatures offer valuable starting points for the early detection of disease-relevant processes. Today, new omic technologies enable the non-invasive detection of epi-proteomic markers from easily accessible samples such as saliva or oral mucosa swabs. Especially saliva, a complex mixture of different biological components, has proven to be a promising medium for the identification of systemic disease markers, including tumor markers. The correlation of biomarkers in saliva with serum parameters underlines the diagnostic potential of saliva-based analyses. In the insurance industry, epi-proteomic data could be used along the entire value chain: in customer acquisition and retention through preventive health programs, in underwriting for more precise risk stratification and in claims management for a more objective assessment of the reintegration ability of customers. Epi-proteomic screenings could thus contribute to individualization and fairness in risk assessment and at the same time enable new prevention-oriented business models. This topic area also shows how insurance companies could expand their social responsibility: Regular, molecular-based health screenings are intended to detect chronic diseases at an early stage and reduce excess mortality. Epi-proteomic methods could play a central role here, as they map early, reversible disease processes and enable individual prevention strategies. This would fundamentally change the traditional role of insurance - from reactive risk carrier to proactive healthcare partner.

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Meanwhile, the use of highly sensitive molecular data poses considerable ethical, legal and regulatory challenges. Data protection, voluntariness and transparency must be central principles of any application of epi-proteomic technologies in the insurance sector. Only through responsible, scientifically sound and socially legitimized use can the full potential of these technologies be exploited for the benefit of individual health and public prevention.

Keywords: Epigenomics, Proteomics, Biomarkers, Risk Assessment, miRNA

## Zusammenfassung

Epigenetische und proteomische Prozesse steuern zentrale biologische Mechanismen und sind dynamisch durch Umwelt- und Lebensstilfaktoren modulierbar. Die Epi-Proteomik - das Zusammenspiel von epigenetischen Modifikationen und proteomischen Veränderungen - eröffnet neue Perspektiven für präventive Ansätze im Gesundheitsmanagement sowie für innovative Anwendungen in der Versicherungswirtschaft. Umweltfaktoren wie Ernährung, körperliche Aktivität und chronischer Stress beeinflussen nachweislich epi-proteomische Muster, was zu langfristigen biologischen Prägungen führt, die beispielsweise in Form eines "epigenetischen Gedächtnisses" von Muskel- oder Fettzellen bestehen bleiben. Diese molekularen Signaturen bieten wertvolle Ansatzpunkte zur frühzeitigen Erkennung krankheitsrelevanter Prozesse. Neue Omic-Technologien ermöglichen heute die nicht-invasive Erfassung epi-proteomischer Marker aus einfach zugänglichen Proben wie Speichel oder Mundschleimhautabstrichen. Besonders Speichel, ein komplexes Gemisch verschiedener biologischer Bestandteile, hat sich als vielversprechendes Medium für die Identifikation systemischer Krankheitsmarker, einschließlich Tumormarker, erwiesen. Durch die Korrelation von Biomarkern im Speichel mit Serumparametern wird das diagnostische Potenzial von Speichel-basierten Analysen unterstrichen. Im Versicherungswesen könnten epi-proteomische Daten entlang der gesamten Wertschöpfungskette eingesetzt werden: in der Kundengewinnung und -bindung durch präventive Gesundheitsprogramme, im Underwriting zur präziseren Risikostratifizierung sowie im Claims-Management zur objektiveren Einschätzung der Wiedereingliederungsfähigkeit erkrankter Versicherter. Epi-proteomische Screenings könnten damit zu einer Individualisierung und Fairness in der Risikoabschätzung beitragen und zugleich neue präventionsorientierte Geschäftsmodelle ermöglichen. Dieser Themenbereich zeigt zudem auf, wie Versicherungsunternehmen ihre gesellschaftliche Verantwortung erweitern könnten: Durch regelmäßige, molekular gestützte Gesundheits-Screenings sollen chronische Erkrankungen frühzeitig erkannt und die Übersterblichkeit gesenkt werden. Epi-proteomische Methoden könnten hier eine zentrale Rolle einnehmen, da sie frühe, reversible Krankheitsprozesse abbilden und individuelle Präventionsstrategien ermöglichen. Damit würde sich das klassische Rollenbild der Versicherung - vom reaktiven Risikoträger zum proaktiven Gesundheitspartner - fundamental wandeln. Die Nutzung hochsensibler molekularer Daten stellen derweil erhebliche ethische, rechtliche und regulatorische Herausforderungen dar. Datenschutz, Freiwilligkeit und Transparenz müssen zentrale Prinzipien jeder Anwendung epiproteomischer Technologien im Versicherungssektor sein. Nur durch einen verantwortungsvollen, wissenschaftlich fundierten und gesellschaftlich legitimierten Einsatz kann das volle Potenzial dieser Technologien im Sinne der individuellen Gesundheit und der öffentlichen Prävention ausgeschöpft werden.

JEL classification: G22, I12

Keywords: Epigenetik, Proteomik, Biomarker, Speichel/Speichelbasierte Diagnostik, Risikobewertung

### 1. Introduction

Biometric insurance policies such as life, health, disability and critical illness insurance are based on statistical risk models that take into account demographic characteristics, medical histories and health-related self-reporting. Although these methods are tried and tested, they are increasingly reaching their limits: The increase in chronic illnesses, demographic change and the expectation of individualized coverage and healthcare are presenting insurance companies with new challenges (Saldanha/Staehle 2023; Stiftung Gesundheitswissen 2022). At the same time, medical research has developed a deeper understanding of the molecular mechanisms of disease development and prevention in recent years – particularly through advances in epigenetics and proteomics (Pigeyre/Yazdi/Kaur/Meyre 2016; Vehmeijer et al. 2020; Wu/Yin 2022). With the help of these advances, the procedural limits for companies could be overcome.

Mechanisms of epigenetics such as DNA methylation and histone modifications influence the expression of genes without changing the underlying DNA sequence. They respond dynamically to environmental factors and lifestyle choices, making them a key link between exposure, behavior and health. Epi-proteomics – as an interface between epigenetics and proteomics – allows the direct detection of functional epigenetic changes in proteins. In contrast to genetic information that is largely static, epi-proteomic markers offer a real-time insight into a person's biological condition. This opens up new possibilities for predictive risk assessment, personalized prevention, personal self-optimization and objective monitoring of the success of health-promoting measures.

Technological progress, especially in the field of mass spectrometry, as well as the increasing availability of minimally invasive sample sources (e.g. blood or oral mucosa) make epi-proteomic analyses practical and affordable for use in applied contexts – including the insurance industry. Pilot projects and initial applications show that epi-proteomic information correlates with clinical parameters, therapy success and health-related behavior. This brings the vision of evidence-based, prevention-oriented and customer-focused insurance medicine within reach.

The aim of this article is to systematically analyze the potential of epi-proteomic methods for the insurance industry. In addition to an introduction to the biological principles, examples of applications, regulatory issues and ethical implications are examined. The focus is on the question of how epi-proteomic markers can contribute to a fair, objective and effective risk assessment – and which prerequisites need to be created for this.

### 2. Epi-proteomics & prevention

Epigenetics is an exciting field of research in biology that deals with the regulation of genes and their inheritance without changing the genetic code itself (Tollefsbol 2023). This means that epigenetic mechanisms can control the activity and use of individual genes. On the one hand, these mechanisms can have short-term effects on the utilization of certain genes, but on the other hand they can also cause permanent, profound changes in the properties of a cell. In recent decades, numerous new mechanisms have been discovered that influence important processes such as DNA repair, transcription and cell division (NHGR Institute 2023). What all processes have in common is that they can be dynamically influenced, in most cases by environmental influences such as exercise, diet, stress and other aspects that have an effect on our bodies. Technological advances have made it possible to analyze the molecular effects and put them into context with each other in order to generate a molecular understanding of lifestyle. The most frequently investigated epigenetic changes are modifications to the DNA itself, to the DNA packaging proteins, so-called histones, and regu-

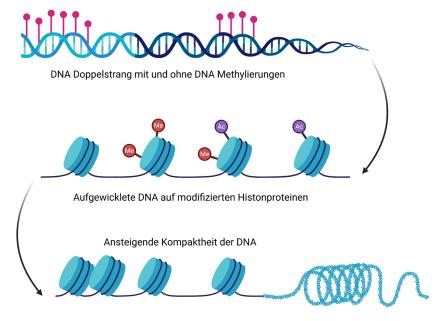


Figure 1: Simplified representation of epigenetic processes in the cell nucleus: DNA can be modified directly at gene segments (pink lollipops) by means of DNA methylation. When the DNA is wound onto so-called histone proteins, regulation can also be achieved via modifications (ME: methylations; Ac: acetylations) take place on the histones. Epigenetic processes influence the winding of DNA into the so-called chromatin and its structure.

lation with the aid of micro RNAs. In DNA methylation, methyl groups are attached to the cytosine base within certain genes, which suppresses the activity of the gene. The methylation pattern changes over the course of a lifetime. Typically, the degree of methylation increases with age and thus leads to the successive silencing of certain gene segments (Figure 1) (Lu et al. 2023). Histones can change the density of DNA organization by adding or removing chemical groups. Such modifications include acetyl, phosphate and methyl groups. This results in a different packaging state of the DNA, which can make it easier or more difficult to read the genes at the DNA level (Figure 1) (Allis/Jenuwein 2016).

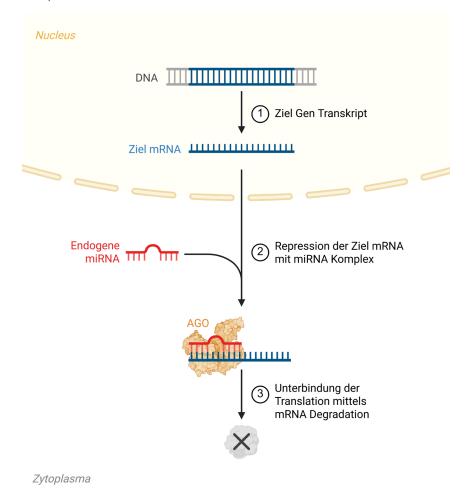


Figure 2: Mechanisms of microRNA regulation as epigenetic regulation of biological processes

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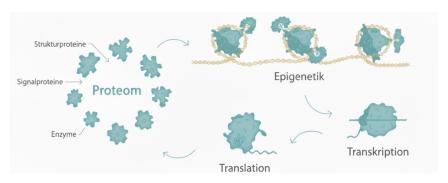


Figure 3: Epi-proteomic relationships in a cell:
Epigenetic processes influence the transcription of genes and ultimately lead to the translation of a gene into a protein. The entirety of all proteins in a cell is referred to as the proteome. Specific proteins in turn cause epigenetic processes and thus lead to a molecular cycle that can often be altered by environmental influences.

MicroRNAs are short RNA molecules that, unlike ordinary RNA strands, are not translated into proteins. Their function is to attach themselves to other RNA molecules and thereby prevent their translation into proteins or even cause the degradation of the RNA molecules (Figure 2) (Moutinho/Esteller 2017).

All epigenetic processes ultimately influence the translation of a gene into the corresponding protein and thus lead to a molecular effect. Proteins are the executive molecular structures in a cell, which perform different functions either individually or as interrelated complexes. Known protein functions include, for example, enzymatic reactions, defense against pathogens or the degradation of obsolete cell materials.

These processes often take place via cascades of several proteins and can also occasionally be self-contained or be organized in amplifying or blocking cycles. This type of self-regulation is also present in epi-proteomics, as certain proteins have the task of carrying out epigenetic changes, such as the methylation of DNA or individual histones. This in turn leads to a compaction of the DNA structure in the cell nucleus and consequently to the silencing of individual genes, so that these genes are no longer translated into the protein responsible for this process (Li/Chen/Lu 2021).

In summary, epi-proteomic mechanisms have a significant influence on genetic processes. While the DNA sequence remains unchanged, epi-proteomic modifications are strongly subject to the effects of environmental factors. For example, DNA methylation, histone modifications and microRNAs show that aspects such as exercise, nutrition and stress have a significant influence on these epi-proteomic mechanisms and thus on cellular processes. For this reason,

we coin the term epi-proteomics in this article, as it is crucial to describe and understand the proteomic effects in addition to the molecular changes at the level of epigenetics. The interaction of these entities allows us to draw medical and health-related conclusions that can be translated into applications.

### 2.1 Epi-proteomics in connection with stress

In 2024, the Nobel Prize in Medicine was awarded to Victor Ambros and Gary Ruvkun for the discovery of microRNA. Their research on nematodes in the 1990s showed that these short RNA segments play an important role in gene regulation (Ambros/Ruvkun 2018). MicroRNAs block the production of certain proteins. Thousands of microRNA genes are now known to be involved in various processes such as embryonic development, mental illness and the development of cancer. In the nerve cells in the brain, they influence our behavior or our reaction to the environment – two processes that are often dysregulated in mental illnesses. Scientists have investigated the role of microRNAs in nerve cells that produce serotonin. Serotonin is a messenger substance that influences, for example, appetite, pain perception or emotions and is also often known as the "happiness hormone". Disorders in the serotonin system are associated with depression or anxiety disorders.

In this context, it has been shown that a specific microRNA called microRNA 135 (miR135) is present in lower quantities than usual in the brain and blood of depressive patients. It reduces the production of two proteins in the serotonin system: SERT (serotonin transporter) and HTR1A (a receptor that inhibits serotonin-producing nerve cells). Less SERT means that less serotonin is transported away, and less HTR1A means less inhibition of serotonin production. Overall, this leads to increased serotonin levels in the brain, similar to the effect of antidepressants, whereby miR135 acts as a kind of endogenous antidepressant (Issler et al., 2014). In another example, it was shown that microRNA 19b (miR19b) is present in increased quantities in certain brain regions of chronically stressed mice. Among other things, it acts on the adrenoreceptor beta-1 (ADRB1), which is activated by noradrenaline and is important for the consolidation of memories. More miR19b leads to less ADRB1, which influences the response to stressors. Mice with more miR19b remembered stressful situations better and showed a more appropriate (less anxious) response when confronted with the stressor again. miR19b thus enables improved stress management (Volk et al. 2014).

In future, the analysis of patients' "microRNA fingerprints" could be used for diagnosis or to determine the treatment strategy. In addition, the development of drugs that increase the amount of protective miRNAs or balance pathologically elevated amounts could open up new therapeutic approaches. Neverthe-

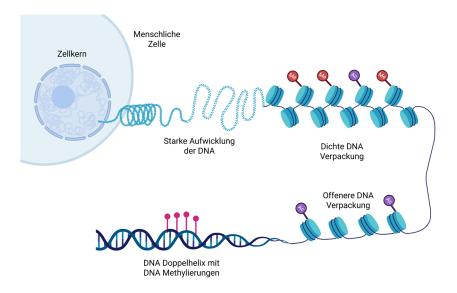


Figure 4: The degree of packaging of genetic information: The large DNA molecule has to be wound up tightly in each cell nucleus. Epigenetic processes, which are used simultaneously to keep the molecule functional, help with this. There are more open gene regions and other more closed gene regions that are not used.

less, a deeper understanding of further epigenetic processes is required to successfully put such therapeutic approaches into practice.

## 2.2 Epi-proteomics in connection with nutrition

The packaging of DNA in the nucleus of eukaryotic cells presents a fascinating challenge. Each cell contains about two meters of DNA, which must be organized into 46 chromosomes. To achieve this compression, the DNA interacts with histone proteins to form nucleosomes. The arrangement of these nucleosomes and the resulting chromatin structure influence access to genes and thus gene expression (Luger/Mader/Richmond/Sargent/Richmond 1997). Histone modifications play a key role in this process. The attachment of acetyl groups loosens the chromatin structure and promotes gene activity, while methyl groups lead to compaction and inhibit gene expression (Jenuwein/Allis 2001).

Current research suggests that these epigenetic mechanisms, and in particular histone modifications, can be modulated by environmental influences such as

diet. For example, new findings from ETH Zurich have shown that fat cells can develop a so-called epigenetic memory for obesity (Hinte et al. 2024).

In studies with mice, the researchers observed that obesity leaves characteristic epigenetic marks in fat cells that persist even after weight loss through dieting. This "memory" of the overweight state facilitated renewed weight gain after returning to a high-fat diet, providing a molecular basis for the yo-yo effect.

The validity of these findings was confirmed by analyzing adipose tissue samples from formerly overweight individuals who had undergone stomach reduction or gastric bypass surgery. Therefore, the researchers emphasize the importance of preventing obesity, especially in childhood and adolescence, as the epigenetic changes in fat cells are long-lived (average lifespan of about ten years) and are currently not reversible by medication. Understanding this epigenetic memory underlines the need to prevent obesity in the first place.

Although this research is the first to demonstrate epigenetic memory in fat cells, it is assumed that other cell types also have such mechanisms. Future studies will investigate whether cells in the brain, blood vessels and other organs also possess such a memory and in which areas it plays a role. The decisive factor here is the technological and computational-analytical ability to detect these biological characteristics and then evaluate them using suitable algorithms. In recent years, major developments have taken place in these areas on the part of data processing, which contribute to the understanding and, above all, the standardized use of such techniques (Abramson et al. 2024).

### 2.3 Epi-proteomic processes in connection with sport and exercise

A team led by biologist Birgitte Regenberg from the University of Copenhagen examined the muscle cells of 16 healthy men aged between 60 and 65. Half of the participants had been active in sports all their lives. The results showed that the genetic material of the athletic men differed from that of the non-athletic men at over 700 DNA sites. In the active older men, genes that code for energy production, muscle building and protection against free radicals were less methylated than in the non-athletic test subjects. This means that these genes are more active and produce more proteins in athletic men (Sailani et al. 2019).

And in this case, too, there are initial findings that these processes could be a kind of molecular memory. During repeated physical exercise, a greater number of hypomethylation was detected at around 18,800 CpG sites compared to around 9,100 CpG sites during the initial strength training exercise. This could be interpreted as a kind of "epigenetic memory" for muscle growth in human skeletal muscle. Nevertheless, further studies are needed to investigate this phe-

nomenon in more detail. Current data on the response to endurance training provide no evidence of such an "epigenetic memory" (Lindholm et al. 2016; Seaborne et al. 2018).

Furthermore, it is clear that epigenetic processes are not solely responsible for the differences. As mentioned at the beginning, the corresponding proteins are also required to implement these changes. A comparison of elite athletes with inactive control subjects shows that genetic differences in enzymes involved in DNA methylation were found in the athletes. This could explain why elite athletes have a higher potential for relative DNA hypomethylation and thus greater muscle growth (Terruzzi et al. 2011).

Overall, the results suggest that exercise generally leads to DNA hypomethylation of important genes in skeletal muscle (Grazioli et al. 2017). This appears to be an early response that supports muscle adaptations to exercise.

Evidence for the influence of sport can also be seen at another level of epigenetics, the histones. Exercise promotes muscle growth and increases metabolism, making cells more sensitive to molecules such as insulin. Studies show that after exercise, cells absorb more glucose because they incorporate more sugar transport proteins into their membranes. Research by Edward Ojuka at the University of Cape Town found that the histones of exercised rats carried more acetyl groups, which led to increased transcription of the glucose transporter gene (Smith/Kohn/Chetty/Ojuka 2008).

In summary, these studies show how important the adaptive response to movement is. The various modifications and signaling pathways indicate a molecular redundancy that has contributed to the survival of organisms over the course of evolution. This requires a comprehensive understanding of molecular processes as well as technologies that map and measure different signaling pathways.

## 3. Epi-proteomic measurements in practice

### 3.1 Overview

In contrast to previous measurements in skeletal muscle and single-molecule analyses, it is now possible to investigate epi-proteomic changes and the molecular players involved, the proteins in easily accessible samples such as oral mucosa swabs and blood. These methods often utilize techniques from drug discovery or biomarker research in the life science and pharmaceutical industries. These methods are designed to measure and determine many analytes simultaneously. This is why they are referred to as omic technologies. The term refers to the collection and analysis of biomarkers in large quantities. Omics include

genomics (DNA), transcriptomics (RNA), proteomics (proteins), lipidomics (fat molecules), glycomics (sugar molecules), metabolomics (metabolism) and interactomics (interaction of molecules). The combination of different omics technologies provides large and very comprehensive data sets that enable a broad analysis of bodily processes. It also has preventative properties, as it is not only possible to search for known disease biomarkers, but also to investigate general metabolic processes. Such an approach can also be used in the insurance industry.

The *MoleQlar Analytics GmbH* examined blood cells and oral mucosal swabs during three months of back training and found that composite epi-proteomic biomarkers obtained from minimally invasive, readily available sample sources (buccal swabs) can accurately reflect an individual's therapeutic status – before and after standardized exercise therapy, despite complex history and lifestyle influences. Improvement in back pain and mobility is associated with a reduction in histone methylation at specific sites, regardless of sample type (buccal cells and PBMCs), which correlate with an increased immune response in plasma. By integrating (objective) molecular changes and (subjective) self-assessment of therapy, a concordance between epi-proteomic profiles and lifestyle categories, underlining the potential of epi-proteomic markers to illustrate the therapeutic pathway of participants (Burny et al. 2024).

Based on these findings, it is also possible to retrospectively understand which people have responded to back therapy and to what extent. This means that this data can be used to create a prospective individual training concept in the future in order to achieve optimal molecular and sports physiological effects of the therapy for each individual person and thus improve overall well-being, freedom from pain and personal health. This case is an example of how an existing therapy concept can be individualised and optimised to improve the fairness and transparency of the claims process and also to develop personalised rehabilitation plans.

In any case, it is clear that sport and exercise cause epigenetic adaptations that can be measured using modern technologies. Most scientific analyses are based on biopsies and laboratory procedures that help to understand molecular mechanisms. In the future, it will be important to use data from simple test systems, such as oral swabs or direct-to-consumer tests, and combine them with other data sources. Technological progress and the processing of large amounts of data require new approaches to data linkage. The example of epi-proteomics shows how complex this topic is and that the integration of diverse data is crucial for a comprehensive understanding. Artificial intelligence could also help to evaluate large amounts of data and recognize patterns at more abstract levels.

### 3.2 The analysis medium saliva

Human saliva is a complex mixture of secretions from the major salivary glands (glandulae salivatoriae majores) and minor salivary glands (glandulae salivatoriae minores), mucosal transudates, exfoliated epithelial cells, gingival sulcus fluid, serum and blood derivatives from oral wounds, coughed up bronchial and nasal secretions, bacteria and their metabolic products, viruses, other cellular components and food residues. Physiologically, this complex mixture also contains hormones, proteins, enzymes, antibodies, antimicrobial components, cytokines and exosomes (Pfaffe/Cooper-White/Beyerlein/Kostner/Punyadeera 2011).

The molecules contained in saliva provide valuable information for clinical diagnostics. Compared to other sample materials such as serum, saliva-based diagnostics offer a number of advantages: in particular, non-invasive and painless sample collection, the small amount of sample required and cost efficiency due to simple storage and uncomplicated transportation (Malathi/Mythili/Vasanthi 2014).

Through the use of new technologies, numerous relevant saliva-based, including epi-proteomic biomarkers for various systemic diseases, including cancer, have been identified (Luedemann et al. 2022). These advances are based on the fact that saliva contains most of the components of serum in a comparable form (Mittal/Bansal/Garg/Atreja/Bansal 2010).

### 4. Biometric insurance

### 4.1 Basic mechanisms

The practice of the insurance industry for biometric risks essentially consists of determining and attributing risks to individuals. These determinations are based almost exclusively on statistical models (Guertin 1965). The assessment of an individual's risk in relation to a particular type of insurance – and thus ultimately the determination of the cost and availability of that insurance – is therefore based on their allocation to certain statistical groups. The assessment of an individual on the basis of such statistical models raises a number of practical questions, e.g. with regard to equity. Palmer (2007) argues that the underlying problem in such cases is how the characteristics of the statistical groups used for insurance purposes can fairly represent the individual as such (Palmer 2007).

The question of fairness – or, more precisely, objectivity and individuality – is far more complex in the context of health. Biometric insurance plays a central role in covering individual risks such as death, illness or disability. The basis of this form of insurance is risk selection, a process in which the individual risk of

potential policyholders is assessed. Traditionally, insurance companies use medical reports, health questionnaires and other relevant data to make informed decisions about whether to accept or reject an insurance application. The aim of the current process is to ensure a fair and sustainable risk assessment that serves the interests of both insurance providers and policyholders (Bender/Nell/Winterhalder 2000).

The risk selection process is influenced by many factors. The information provided by the applicant forms the basis for the decision-making process. In today's process, the applicant is generally required to provide information on their personal medical history over the last 3-10 years (depending on the insurance provider and question category). Complete documentation is an essential factor, also with regard to the statutory pre-contractual duty of disclosure (VVA). This already illustrates the complexity of a fair and objective assessment in the field of biometric insurance. Based on this process, the challenge of information asymmetry is eminent in the risk assessment of biometric risks (Dicke 2004). While with some other insurance products it can be assumed that the insured person and the insurance company have the same information about factors influencing the future risk, the insured person may have an information advantage in biometric insurance. A typical manifestation of information asymmetry in insurance is anti-selection, which in economics always occurs when one party possesses information prior to a transaction that would change the basis of the transaction if both parties had possessed this information in advance (Dicke 2004).

Another central mechanism of biometric insurance is pricing, i.e. the determination of insurance premiums. These are based on statistical models that take into account demographic factors, health conditions and individual risk profiles. Correct premium calculation is essential to ensure the economic stability of the insurer on the one hand and fair premiums for the insured on the other insured persons. Challenges arise here primarily due to uncertainties in the risk forecast, for example as a result of incomplete or incorrect data, as well as changes in the state of health of the insured persons during the term of the contract (Blankart/Fasten/Schwintowski 2009).

Biometric insurance is therefore faced with the task of developing precise risk selection and pricing strategies on the one hand and dealing with the challenges arising from potential data gaps, ethical issues and compliance with regulatory requirements on the other. This paper examines the mechanisms and problems of risk selection and premium setting and explores how these processes can be optimized through technological innovation and improved data integrity.

## 4.2 Current developments in the field of biometric insurance

The biometric insurance industry is currently undergoing a profound transformation process characterized by technological advances and changing customer requirements (Hach et al. 2024). One key trend is the increased focus on preventive measures. Insurance companies are increasingly recognizing that they not only offer financial protection in the event of a claim, but can also actively contribute to promoting the health of their policyholders. Disease prevention programs based on the analysis of individual health data are becoming increasingly relevant. The use of wearables, health applications and personalized coaching offers supports policyholders in leading a healthy lifestyle and reducing potential health risks (Weis 2024).

Another key area of development is the digitalization of insurance services. Policyholders increasingly expect integrated, digital solutions that provide easy access to policies and health information. Mobile applications that create transparency about insurance benefits and at the same time provide proactive health information represent significant added value for many customers. In addition, digital platforms allow insurance companies to establish continuous interaction with policyholders, which helps to strengthen customer loyalty in the long term (Hornung 2024).

At the same time, policyholders are increasingly expecting direct benefits from the premiums they pay. In this context, so-called value-added services are gaining in importance. These additional services go beyond the traditional insurance approach and offer customers added value that directly improves their quality of life. Examples include discounts on gym memberships, access to telemedicine services or premium refunds for demonstrably healthy behavior. These services not only help to increase customer satisfaction, but can also reduce the use of insurance services in the long term (Brophy 2013).

However, the implementation of value-added services places new demands on the existing infrastructure and the strategic orientation of insurance companies. In addition to investments in innovative technologies, strict data protection regulations must be adhered to in order to maintain customer trust. It is also necessary to design these services in such a way that they offer sustainable long-term benefits from both the customer's and the company's perspective.

## 4.3 The role of epigenetic methods in risk stratification in the insurance industry

Advances in epigenetics open up new perspectives for individual risk assessment and prevention in the insurance context. The possibility of using epi-proteomic methods to gain deeper insights into the dynamic health status of an

individual means that epi-proteomics is becoming increasingly important for insurance models based on a more precise assessment of morbidity and mortality risks. This dynamic level of biological regulation is highly relevant for insurance medicine. This is because it enables not only a retrospective analysis of exposures, but also the prospective assessment of disease risks in real time. In this way, specific epi-proteomic patterns can be correlated with the occurrence of chronic degenerative diseases such as cardiovascular diseases, neurodegenerative diseases or malignant tumors. In this sense, epi-proteomics extends the spectrum of risk assessment beyond static characteristics (e.g. age, family history, smoking status) to include biologically highly sensitive markers that map the individual risk of morbidity and mortality in a more differentiated way.

For insurance models – especially in life, health, disability or critical illness insurance – this means a new quality of risk stratification. In future, the integration of epi-proteomic data could make it possible to define more precise risk classes, identify early indicators for pathophysiological processes and develop personalized prevention strategies. In this way, insurers could not only better calculate risks, but also proactively contribute to health maintenance – for example through targeted prevention programs for high-risk groups whose molecular risk signatures have already been detected before clinical symptoms appear.

### 4.3.1 Life insurance

In the field of life insurance, epigenetic age determination can be used as an indicator of biological ageing. Studies show that epigenetic age correlates significantly with overall mortality, but also with cardiovascular, metabolic and oncological diseases. Accelerated epigenetic age acceleration could therefore serve as a predictive biomarker in insurance medical risk assessment – provided that regulatory and ethical framework conditions are appropriately taken into account (Fransquet/Wrigglesworth/Woods/Ernst/Ryan 2019; Gibson et al. 2019).

In addition, the difference between biological and chronological age opens up a new understanding of individual vulnerability that goes beyond traditional socio-demographic risk models. People with a significantly "advanced" epigenetic age could – regardless of their calendar age – have an increased risk of premature morbidity and mortality. This discrepancy can be interpreted as a molecular biological marker for so-called "hidden risks" that are not or only insufficiently captured by conventional underwriting methods. At the same time, epigenetic age offers a dynamic and modulable risk marker. Studies show that certain lifestyle factors such as diet, exercise or stress management can cause a measurable slowdown or even reversal of epigenetic ageing. The work of Hannum et al. showed that ageing is associated with specific changes in DNA methylation and that these can be used as reliable biomarkers to determine biological

age (Hannum et al. 2013). This is an aspect that is important not only for risk assessment, but also for health-promoting insurance models (e.g. bonus programs or prevention tariffs) are likely to become increasingly relevant.

### 4.3.2 Income protection

Epi-proteomics also has potential for occupational disability insurance. The epi-proteomic signatures, which reflect cumulative stresses such as chronic stress, sleep deprivation or environmental toxins associated with functional limitations and mental illness, can help to identify insured persons with an increased risk of stress-associated disorders or chronic fatigue – two of the main reasons for occupational disability claims. In combination with psychometric data, they could enable preventive interventions in the medium term.

The systematic integration of epi-proteomic risk profiles into insurance medical models could significantly improve the early detection of psychosomatic or functional illnesses. At the same time, this opens up the opportunity to reach insured persons with incipient but still reversible biological changes at an early stage and to prevent the threat of occupational disability through targeted measures such as coaching programs, resilience promotion or occupational health interventions. In the long term, this could not only reduce the individual risk of illness, but also have a positive impact on the benefit ratio of occupational disability insurers.

#### 4.3.3 Health insurance

In health insurance, epi-proteomics enables a transition from reactive to proactive care. Epi-proteomic profiles could be used to design personalized prevention programs, for example for diabetes, COPD or neurodegenerative diseases. Especially in systems with managed care or bonus programs, there is an opportunity to manage preventive measures based on evidence and evaluate their effectiveness using molecular markers. Initial studies show that epi-proteomic patterns can be changed by lifestyle interventions, which offers a direct starting point for health-promoting programs.

In addition, longitudinal epi-proteomic analyses enable continuous monitoring of the state of health – a potential paradigm shift in care management. Instead of only reacting to manifest symptoms, insurers could use digital health platforms to integrate epi-proteomic early warning systems that indicate inflammatory processes or metabolic dysregulation, for example. This would make it possible to initiate risk-adapted measures in good time and reduce costs due to later chronic processes. At the same time, biofeedback-type feedback on the effect of lifestyle changes could motivate insured persons to improve their behav-

ior in the long term. This would allow a new understanding of prevention based on molecular evidence to be established, which would improve both the medical quality and cost-effectiveness of care.

### 4.3.4 Critical illness insurance

Epi-proteomics offers a promising approach to early diagnosis and risk profiling for critical illness insurance, which focuses on coverage for serious diagnoses such as cancer, heart attack or stroke. For example, epigenetic blood tests for the detection of pre-symptomatic tumor stages are in advanced development (Beltran-Garcia/Osca-Verdegal/Mena-Molla/Garcia-Gimenez 2019; Jones/Baylin 2002). Studies also show that potential customers are even positive about predictive tests (Wegwarth/Pashayan/Widschwendter/Rebitschek 2019). Inflammatory and metabolic diseases can also be detected via specific epi-proteomic signatures, thus enabling a potential paradigm shift in underwriting practice: from retrospective to predictive risk (Martinez/Gay/Zhang 2015; Wu/Yin 2022).

Epiproteomic methods not only allow early detection of tumor diseases with high sensitivity and specificity (Van den Ackerveken et al. 2021), but could also be used in the future for risk stratification for cardiovascular events – for example via epigenetic markers of endothelial dysfunction or chronic inflammation. For insurers, this opens up the possibility of identifying at a molecular level those people who are still clinically asymptomatic but have a significantly increased risk of serious illness. In the future, such information could also be incorporated into the development of dynamic policy models that incorporate preventive behavior and molecular risk reduction into the premium structure, provided the appropriate data protection regulations are in place. In this way, critical illness insurance could not only protect, but also actively contribute to disease prevention.

## 5. Integration of epi-proteomic analyses into the value chain of an insurance company

The integration of epi-proteomic methods in the field of biometric insurance would undoubtedly be an innovative step in the use of epi-proteomic analyses for the insurance sector. The aim will be to translate the potential of epi-proteomic information into usable and understandable added value for insurance customers. Epiproteomics can play a role in various parts of an insurer's value chain:

### 5.1 Lead generation and retention

In the area of customer acquisition, insurers can position personalized health analyses based on epi-proteomic profiles as part of preventive service offerings. For example, life, health or disability insurers can offer health checks that use epi-proteomic tests to detect not only traditional risk factors, but also early indications of regenerative capacities or disease risks. Such an offer differs significantly from conventional health checks and signals innovation, individual appreciation and active health promotion – aspects that are particularly relevant for health-conscious, well-informed target groups.

The regular performance of such tests opens up further opportunities in terms of customer loyalty. Insurers could develop programs that offer prevention or coaching measures based on individual epi-proteomic status. This means that customers not only receive an insurance benefit in the event of a claim, but also continuous support in maintaining and improving their health. Such programs strengthen the emotional bond with the company and significantly increase the barriers to switching. In addition, longitudinal epi-proteomic analyses enable personalized interactions and offers that go beyond generic customer approaches.

Responsible handling of highly sensitive health data is key to successful integration. The collection and use of epi-proteomic information must be transparent, voluntary and earmarked. Data protection-compliant processes and clear value-added communication are crucial to creating trust and ensuring customer acceptance.

### 5.2 Underwriting

Medical underwriters routinely arrange for blood and urine tests, depending on the age of the applicant, the desired insurance product and the sum insured applied for. In rare cases and in response to a specific question, non-routine or discretionary tests may also be requested to clarify medical uncertainties. Several criteria are carefully considered before deciding on routine or special tests (Dicke 2004).

It plays a role in whether the test is able to reliably detect health impairments with relevant effects on mortality or morbidity. The cost-benefit ratio is also taken into account. Equally important is whether the test has been tested and recognized in the medical community. Another aspect is practical feasibility in the laboratory: the test must be easy to perform, precise, reproducible and economically scalable.

It also assesses whether the disease to be examined occurs sufficiently frequently in the insured population to justify the costs of broad screening. The test is intended to improve the fairness of risk assessment by enabling people to be assigned to the appropriate risk categories as accurately as possible. Last but not least, the potential benefits for applicants are also considered: The use of such tests can help to keep insurance products affordable and accessible for the majority of customers (Daniel/Kita 1998).

A widely used marker for risk stratification in underwriting is cotinine, which, as a degradation product of nicotine, is used as a "long-term marker" to test smoking behavior and, if necessary, to integrate it into the pricing of the desired insurance product. First of all, it should be noted that cotinine is a reliable marker for tobacco smoke exposure in terms of sensitivity and specificity. Nevertheless, there are limitations and challenges, particularly for the risk assessment process:

- It is difficult to determine universal cut-off values for cotinine that reliably distinguish between active smokers, passively exposed non-smokers and non-exposed non- smokers. Differences in the individual metabolization of nicotine and cotinine make it difficult to establish uniform cut-off values (Haufroid/Lison 1998).
- People who use nicotine replacement products such as patches or chewing gum may have elevated cotinine levels even though they do not consume tobacco. This can lead to misclassification, especially in smoking cessation studies or programs (Hurt et al. 1993).
- 3. The half-life of cotinine is about 16 to 20 hours, which means that it mainly reflects tobacco smoke exposure over the last 1 to 3 days. This may limit the assessment of long-term exposure patterns (Benowitz 1996).

With epi-proteomic markers, insurers would be able to assess and adequately price smoking behavior (Kaur/Begum/Thota/Batra 2019), as studies have shown that epi-proteomic methods are suitable for this purpose and meet the requirements of the insurance industry (Poussin et al. 2024; Wrzesniak/Kepinska/Krolik/Milnerowicz 2016). *MoleQlar Analytics*' own unpublished data confirm that so-called multifactorial epi-proteomic markers are well suited for determining smoking status and even classifying the type of smoking/vaping (smoking, e-cigarette, vaping, etc.). These data are also based on non- invasive cheek swabs and are therefore quick and easy to use in practice and can thus transform a previously binary decision (smoker vs. non-smoker) into a granular health analysis (light vs. heavy smoker; non-smoker, vaper, e-cigarette user). Especially since the molecules consistently found in the various studies are also frequently described in ageing processes and thus allow conclusions to be drawn about morbidity and mortality. In this context, it is molecularly verifiable that increased

markers in smoker cohorts also prove an advanced ageing process in these groups of people. These findings can therefore be linked quite quickly to the insurance industry's calculation models. Due to the current cost structure of epi-proteomic test procedures, this makes sense in terms of cost-benefit considerations, especially for higher insurance sums.

### 5.3 Claims management

Claims management is a central function in the value chain of an insurance company, which not only includes claims settlement, but increasingly also the active support of insured persons in their return to work. Epi-proteomic test procedures offer deeper insights into disease activity, regeneration potential and individual prognoses than traditional clinical markers. In the claims area, these technologies can be used in particular by disability and health insurance companies to make reliable, individualized statements about the ability of sick customers to return to work. While traditional medical reports often represent a snapshot in time, epigenetic and proteomic data provide objective, quantifiable parameters. For example, epigenetic ageing markers can provide information on the actual biological burden of an insured person, while certain protein signatures predict the course of chronic illnesses or recovery after acute illnesses.

By integrating these tests into the claims process, the insurance company can not only improve the fairness and transparency of the benefit assessment, but also develop personalized rehabilitation plans. This promotes faster and more sustainable reintegration into working life and reduces long-term benefit payouts. In addition, a data-driven approach can strengthen customer trust and position the company as an innovative partner in healthcare management. At the same time, ethical, data protection and regulatory aspects must be strictly observed. The voluntary consent of the insured person, the purpose limitation of the test data and the observance of proportionality must be central principles. Only through responsible

Utilization of these technologies allows their full potential to be exploited in claims management.

Overall, epigenetic and proteomic tests offer a promising addition to classic methods for assessing the reintegration ability of sick insured persons and thus contribute to increasing efficiency and customer orientation in claims management.

## 5.4 Data translation: from science to customer value

The biggest challenge for integration into any part of the value chain was to translate the complex results of the epi-proteomic analyses into a language that is understandable and valuable for policyholders. The following approaches could be helpful here:

- 1. Data visualization: Development of intuitive dashboards and visualizations that show individual health risks and recommendations for action.
- 2. *Narrative science*: creating narrative scenarios to help clients understand the importance of epi-proteomic information to their health and lifestyle.
- Validation through user testing: Customer surveys and focus groups were conducted to ensure that the information provided was understandable and useful.

Beyond the traditional business models of the insurance industry, which traditionally consist of the development and marketing of standardized insurance products and services, the integration of epi-proteomic analyses opens up significant potential to fundamentally expand the role of insurance companies (Nodine 2024). Epi-proteomic methods, which can provide precise and dynamic information about an individual's state of health, enable insurers to transform their traditionally reactive business model – financial protection in the event of a claim – into a proactive and prevention-oriented paradigm.

In future, insurance companies could play an active role in shaping health by establishing regular molecular screenings and developing holistic prevention and intervention services on this basis. Such screenings could be carried out using epi-proteomic methods could not only identify classic risk factors, but also early molecular signatures of subclinical disease processes, thus enabling preventive action to be taken even before manifest diseases develop. This would mean a fundamental shift in the role of insurance companies: from a pure risk carrier to an active partner in individual healthcare. The Insurance Collaboration to Save Lives initiative is particularly relevant in this context. This nonprofit organization, founded by leading representatives of the international insurance and healthcare industry, aims to enable insurance companies worldwide to offer regular health screenings, tests and triage procedures for their policyholders (Stirling 2024). The initiative is a response to the globally observed increase in excess mortality, particularly in connection with chronic degenerative diseases, which can often be diagnosed at the molecular level long before clinical manifestation.

The Insurance Collaboration to Save Lives approach is an example of how insurers can not only improve individual quality of life through systematic, evidence-based prevention programs, but also live up to their social responsibility.

The integration of regular molecular health checks – ideally taking into account modern epi-proteomic technologies – could be an effective mechanism for reducing health disparities, lowering the incidence of chronic diseases and thus making a substantial contribution to public health.

In addition, such a strategy would further strengthen the role of insurers as trusted custodians of highly sensitive health data. Insurance companies traditionally have a long history of handling personal data responsibly. This basis of trust could be used to anchor innovative preventive services in society and establish a new dimension of solidarity within the insurance collective.

It turns out that the combination of technological innovation (epi-proteomic processes) and structural realignment opens up the possibility of fundamentally transforming the insurance business: from a primarily transactional system of risk protection to an integrative, health-promoting and socially shaping player.

Despite the promising prospects, there are key challenges to consider. The use of epigenetic data in the insurance context raises fundamental ethical and data protection issues. In addition, the translation of epi-proteomic research results into clinically and actuarially validated applications is still in the early stages. Nevertheless, there are indications that epi-proteomic methods could play a key role in the long term in more precise, fairer and more prevention-oriented insurance medicine – especially in the context of individualized risk and health care.

### 6. Critical analysis of epi-proteomic data in insurance

Schuol et al. (2015) examine the various problem areas and conflicts of interest associated with the use and exploitation of epigenetic data. In particular, they focus on the tensions between the various social actors, each of whom pursue divergent goals and expectations. Epigenetic data is of particular interest to various groups, including scientists, political decision-makers, medical institutions and private insurance companies. These diverging interests create a field of tension in which ethical, legal and social aspects play a central role (Schuol/Rockoff/Ranisch 2015).

In a recent publication, Dupras et al. examine the views of epigenetics researchers on ethical, legal and social aspects (ELSI) in their field of research (Dupras et al. 2022). Between January and March 2020, an online survey was conducted among 189 epigenetics researchers from 31 countries. Participants were asked about their understanding of the field, opportunities in different areas of specialization, and ELSI issues in research and knowledge transfer. They were also asked to rate their concerns about four emerging non-medical applications of epigenetic testing – in life insurance, forensics, immigration and direct-to-consumer testing. The most common ELSI issues experienced or ob-

served by respondents were related to timely access to epigenetic data in existing databases and communication of epigenetic results by the media. Researchers also expressed great concern about non-medical applications of epigenetics, which is consistent with cautious assessments in the humanities and social science literature.

Private insurance companies could belong to these non-medical areas of application and are often perceived as purely profit-oriented players in the health-care sector. Their primary objective of making a profit is essential for the continued existence of the company. At the same time, this profit motive is in tension with their social responsibility to ensure the accessibility and affordability of insurance for as many individuals as possible. Interestingly, however, the insurance business model is based on a principle of solidarity per se: the equalization of individual risks via the collective. In this context, the increasing objectifiability of health through the use of epigenetic data could offer considerable advantages for the insurance industry and society as a whole.

If epigenetic information helps to improve the predictivity and prevention of diseases, this could have positive effects that benefit both the insured community and insurance companies. Accurate and well-founded predictions could, for example, lead to more targeted preventive measures, which in turn would reduce healthcare costs in the long term. Lower costs mean potentially lower premiums for policyholders, which not only increases the attractiveness of the insurance offer, but also enables other social groups to participate. In this way, the solidarity-based model is strengthened by involving a larger proportion of the population in collective risk management.

However, the exploitation of such data also harbors risks, such as the danger of discrimination or the violation of data protection. This raises the question of how a balance can be struck between the commercial interests of insurers, social responsibility and the protection of individual privacy. Schuol et al. (2015) emphasize that these issues cannot be considered in isolation, but require an integrative approach that takes ethical, social and legal perspectives into account.

## 7. Regulatory framework for the use of genetic and epigenetic data in the private insurance industry

The use of genetic and epigenetic data in the private insurance industry is caught between technological progress, data protection and ethical issues. Regulatory requirements vary greatly between different countries and jurisdictions. Genetic data in particular is strictly regulated in many jurisdictions, while epigenetic data, which can be modified by environmental influences and lifestyle changes, is not always explicitly included in the legal framework. The legislation

in Germany, the EU, the UK, the US and more liberal markets is summarized below.

### 7.1 Focus regions

## 7.1.1 Germany

In Germany, the Genetic Diagnostics Act (GenDG) regulates the use of genetic data. It largely prohibits insurance companies from accessing genetic test results. There is an exception for high insurance sums (usually over 300,000 euros), although strict conditions apply here too. Epigenetic data is not yet explicitly covered by the GenDG, but could be subsumed under general data protection law (GDPR) as it allows conclusions to be drawn about an individual's health.

### 7.1.2 European Union

At EU level, the General Data Protection Regulation (GDPR) forms the central framework for the protection of genetic data. According to Article 9 GDPR, genetic data are classified as special categories of personal data and their processing is generally prohibited unless there is explicit consent from the data subject or a legal basis. Epigenetic data could also fall under this category if it is used for identification or profiling. However, national differences in the implementation of the GDPR lead to inconsistent handling of this data.

### 7.1.3 United Kindgom (UK)

After leaving the EU, the Data Protection Act 2018 (DPA) applies in the UK, which is largely based on the principles of the GDPR. Similar protection provisions apply to genetic data as in the EU. The Association of British Insurers (ABI) has reached a voluntary agreement under which genetic tests may only be used in exceptional cases for life insurance policies with high sums insured. Epigenetic data is not yet specifically regulated, but could fall under general data protection regulations.

### 7.1.4 United States of America (USA)

In the USA, the Genetic Information Nondiscrimination Act (GINA) regulates the use of genetic data. GINA prohibits employers and health insurers from using genetic information to make decisions about hiring, promotion or insur-

ance coverage. However, life and disability insurance are not covered by GINA, so insurers can use this data under certain conditions. Epigenetic data is not explicitly covered by GINA and can therefore potentially be used more broadly, subject to the general privacy laws of individual states such as the California Consumer Privacy Act (CCPA).

### 7.1.5 More liberal markets

In more liberal markets such as Australia or Singapore, the use of genetic data is less strictly regulated. In Australia, insurance companies can use genetic test results for risk assessment, provided the data is relevant and proportionate. Epigenetic data is not usually treated separately in law, which facilitates wider use in practice. Singapore has similar approaches, with a focus on self-regulation of the insurance industry.

## 7.2 Challenges and future prospects

The increasing availability and accuracy of epigenetic data raises new questions that existing regulatory frameworks do not always cover. While genetic data is largely considered static, epigenetic information offers dynamic insights into a person's health and lifestyle. This flexibility could offer insurance companies on the one hand new opportunities for risk assessment on the other hand, also entail considerable ethical and data protection challenges.

The harmonization of legal regulations and the consideration of epigenetic data in existing frameworks will be crucial to ensure responsible and fair handling of this sensitive information. The implementation of the approaches described in this article is still in its infancy and needs to be underpinned by further studies and clinical investigations. On the other hand, the fields of laboratory analysis and data processing are developing exponentially, so that larger amounts of data from the fields of epigenetics and proteomics are already available and can be processed together. Looking ahead, it can be assumed that the first pilot applications in the insurance industry will be observed over the next few years in order to be able to test the full application in the value chain. In this context, we expect to see more partnerships between established insurance companies and young data-driven companies in the field of diagnostics and health in the future.

### **Summary**

The article highlights the central role of epigenetic and proteomic processes in the molecular regulation of gene activity and their significance for the prevention of chronic diseases. Building on established mechanisms such as DNA methylation, histone modifications and microRNA interactions, a comprehensive picture of the dynamic nature of epigenetic processes is presented. In contrast to the unchanging DNA sequence, epigenetic changes provide a flexible, environmentally influenced level of biological control that significantly influences the proteome – the totality of proteins produced in a cell.

The term epi-proteomics is coined to describe the reciprocal influence of epigenetic changes on protein expression and vice versa. Proteins not only act as effectors of epigenetic regulation, but also modulate epigenetic processes themselves, resulting in complex feedback systems in cell regulation.

In the context of chronic stress, the article uses microRNAs such as miR135 and miR19b to illustrate the role of epigenetic modulations in the regulation of stress responses and affective disorders. These mechanisms open up perspectives for new diagnostic and therapeutic approaches in the field of mental illness.

Dietary factors have also been shown to have profound effects on epigenetic patterns. The discovery of an "epigenetic memory" in fat cells underlines that obesity leaves molecular traces that can increase the risk of later weight gain despite weight loss. Such findings emphasize the importance of preventive measures starting in childhood.

In the field of sport and exercise, studies demonstrate that regular physical activity is associated with sustained hypomethylation of certain genes in skeletal muscle. This postulates an "epigenetic muscle memory" that could offer long-term benefits for muscular function and metabolism.

The article points out that modern omic technologies now make it possible to obtain epi-proteomic markers non-invasively from easily accessible samples such as blood or oral mucosa. This opens up new fields of application, particularly for biometric insurance models.

In the area of customer acquisition and retention, insurers could offer preventive health checks based on epi-proteomic profiles. Such individualized services differentiate insurance products in the market, promote customer loyalty through continuous health monitoring and create added value through personalized prevention.

In the underwriting process, epi-proteomic markers could contribute to more precise risk stratification. Similar to established markers (e.g. cotinine for nicotine consumption), epi-proteomic profiles could objectify risk factors such as biological ageing, chronic inflammatory processes or metabolic dysfunctions and thus enable differentiated pricing. Due to current cost structures, its use is primarily recommended for higher sums insured.

In claims management, epi-proteomic tests offer new opportunities to individually and objectively assess the ability of insured persons to return to work after illness. They enable a dynamic assessment of regeneration processes and disease activity and could thus support the development of personalized rehabilitation plans. In the long term, they could help to optimize benefit payments and promote a sustainable return to work.

The use of epi-proteomic data in the insurance context raises significant ethical and regulatory issues. Data protection, voluntary consent and transparent communication of the added value for the insured person are essential. In addition, the clinical validation of many epi-proteomic markers is still in progress, which is why responsible and scientifically sound implementation must be a top priority. At the same time, the responsible use of these technologies could transform the insurance business in the long term: away from purely reactive risk protection towards a prevention- oriented, health-promoting partnership between insurer and customer.

Epi-proteomics offers a promising set of tools to better capture individual health conditions and lifestyle influences. Its integration into the value chain of biometric insurance – from customer acquisition and underwriting to claims management – could open up considerable potential for innovation. However, this requires a balanced, ethical handling of the data obtained that respects both the interests of the insurance companies and the protection and autonomy of the insured persons. To bring this potential to life, further interdisciplinary collaboration is needed between researchers, insurers, regulators, and ethicists. Pilot projects and controlled studies can help explore practical applications, while clear frameworks for data governance and transparency must be established to build trust and ensure responsible use.

### References

Abramson, J./Adler, J./Dunger, J./Evans, R./Green, T./Pritzel, A./... Jumper, J. M. (2024): Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature, 630(8016), 493 – 500. doi:10.1038/s41586-024-07487-w.

Allis, C. D./Jenuwein, T. (2016): The molecular hallmarks of epigenetic control. Nat Rev Genet, 17(8), 487 – 500. doi:10.1038/nrg.2016.59.

Ambros, V./Ruvkun, G. (2018): Recent Molecular Genetic Explorations of Caenorhabditis elegans MicroRNAs. Genetics, 209(3), 651 – 673. doi:10.1534/genetics.118.300291.

- Beltran-Garcia, J./Osca-Verdegal, R./Mena-Molla, S./Garcia-Gimenez, J. L. (2019): Epigenetic IVD Tests for Personalized Precision Medicine in Cancer. Front Genet, 10, 621. doi:10.3389/fgene.2019.00621.
- Bender, K./Nell, M./Winterhalder, H. (2000): Die Finanzierungsfunktion der Lebensrückversicherung: Rückdeckung plus Kontokorrentkredit. VW, 55, 171.
- Benowitz, N. (1996): Cotinine as a Biomarker of Environmental Tobacco Smoke Exposure. Epidemiologic Reviews, 18(2).
- Blankart, C. B./Fasten, E./Schwintowski, H.-P. (2009): Das deutsche Gesundheitswesen zukunftsfähig gestalten: Patientenseite stärken Reformunfähigkeit überwinden. Berlin: Springer.
- *Brophy*, R. (2013): Adding value to insurance products: The AXA Irish experience. Journal of Product & Brand Management, 22(4), 293 299.
- Burny, C./Potocnjak, M./Hestermann, A./Gartemann, S./Hollmann, M./Schifferdecker-Hoch, F./... Voelker-Albert, M. (2024): Back pain exercise therapy remodels human epigenetic profiles in buccal and human peripheral blood mononuclear cells: An exploratory study in young male participants. Front Sports Act Living, 6, 1393067. doi:10.3389/fspor.2024.1393067.
- Daniel, P./Kita, M. W. (1998): Drawing Conclusions From Test Results. In: Elder, W. J./ Brackenridge, R. D. (Eds.), Medical Selection for Life Risks, Vol. 4, 233 – 248. Hamp-shire, UK: Stockton Press.
- Dicke, A. A. (2004): The Economics of Risk Selection. In: Rothstein, M. A. (Ed.), Genetics and Life Insurance Medical Underwriting and Social Policy, 49 50. Boston: Massachusetts Institute of Technology.
- Dupras, C./Knoppers, T./Palmour, N./Beauchamp, E./Liosi, S./Siebert, R./... Joly, Y. (2022): Researcher perspectives on ethics considerations in epigenetics: an international survey. Clin Epigenetics, 14(1), 110. doi:10.1186/s13148-022-01322-7.
- Fransquet, P. D./Wrigglesworth, J./Woods, R. L./Ernst, M. E./Ryan, J. (2019): The epigenetic clock as a predictor of disease and mortality risk: A systematic review and meta-analysis. Clin Epigenetics, 11(1), 62. doi:10.1186/s13148-019-0656-7.
- Gibson, J./Russ, T. C./Clarke, T. K./Howard, D. M./Hillary, R. F./Evans, K. L./... Marioni, R. E. (2019): A meta-analysis of genome-wide association studies of epigenetic age acceleration. PLoS Genet, 15(11), e1008104. doi:10.1371/journal.pgen.1008104.
- Grazioli, E./Dimauro, I./Mercatelli, N./Wang, G./Pitsiladis, Y./Di Luigi, L./Caporossi, D. (2017): Physical activity in the prevention of human diseases: role of epigenetic modifications. BMC Genomics, 18(Suppl 8), 802. doi:10.1186/s12864-017-4193-5.
- Guertin, A. N. (1965): Life Insurance Premiums. The Journal of Risk and Insurance, 32(1), 23-49.
- Hach, W./Stark, S./Basten, D./Windhager, T./Biernatzki, W./Thews, J. (2024): Die "überfällige" Transformation der Versicherungskernsysteme [Press release].
- Hannum, G./Guinney, J./Zhao, L./Zhang, L./Hughes, G./Sadda, S./... Zhang, K. (2013): Genome-wide methylation profiles reveal quantitative views of human aging rates. Mol Cell, 49(2), 359 367. doi:10.1016/j.molcel.2012.10.016.

- Haufroid, V./Lison, D. (1998): Urinary cotinine as a tobacco-smoke exposure index: A minireview. International Archives of Occupational and Environmental Health, 71, 162 – 168.
- Hinte, L. C./Castellano-Castillo, D./Ghosh, A./Melrose, K./Gasser, E./Noe, F./... von Meyenn, F. (2024): Adipose tissue retains an epigenetic memory of obesity after weight loss. Nature, 636(8042), 457 – 465. doi:10.1038/s41586-024-08165-7.
- Hornung, A. (2024): Die Customer Journey der Zukunft: Was erwarten Kunden von ihrer Versicherung? Cash. Retrieved from https://www.cash-online.de/a/die-customer-jour ney-der-zukunft-oder-was-erwarten-kunden-von-ihrer-versicherung-688929/#comments.
- Hurt, R. D./Dale, L. C./Offord, K. P./Lauger, G. G./Baskin, L. B./Lawson, G. M./... Hauri,
  P. J. (1993): Serum nicotine and cotinine levels during nicotine-patch therapy. Clin Pharmacol Ther, 54(1), 98 106. doi:10.1038/clpt.1993.117.
- Issler, O./Haramati, S./Paul, E. D./Maeno, H./Navon, I./Zwang, R./... Chen, A. (2014): MicroRNA 135 is essential for chronic stress resiliency, antidepressant efficacy, and intact serotonergic activity. Neuron, 83(2), 344 360. doi:10.1016/j.neuron.2014.05.042.
- Jenuwein, T./Allis, C. D. (2001): Translating the histone code. Science, 293(5532), 1074-1080. doi:10.1126/science.1063127.
- *Jones*, P. A./*Baylin*, S. B. (2002): The fundamental role of epigenetic events in cancer. Nat Rev Genet, 3(6), 415 428. doi:10.1038/nrg816.
- Kaur, G./Begum, R./Thota, S./Batra, S. (2019): A systematic review of smoking-related epigenetic alterations. Arch Toxicol, 93(10), 2715-2740. doi:10.1007/s00204-019-02562-y.
- *Li*, Y./*Chen*, X./*Lu*, C. (2021): The interplay between DNA and histone methylation: molecular mechanisms and disease implications. EMBO Rep, 22(5), e51803. doi:10.15252/embr.202051803.
- Lindholm, M. E./Giacomello, S./Werne Solnestam, B./Fischer, H./Huss, M./Kjellqvist, S./ Sundberg, C. J. (2016): The Impact of Endurance Training on Human Skeletal Muscle Memory, Global Isoform Expression and Novel Transcripts. PLoS Genet, 12(9), e1006294. doi:10.1371/journal.pgen.1006294.
- Lu, A. T./Fei, Z./Haghani, A./Robeck, T. R./Zoller, J. A./Li, C. Z./... Horvath, S. (2023): Universal DNA methylation age across mammalian tissues. Nat Aging, 3(9), 1144–1166. doi:10.1038/s43587-023-00462-6.
- Luedemann, C./Reinersmann, J. L./Klinger, C./Degener/S./Dreger, N. M./Roth, S./... Savels-bergh, A. (2022): Prostate Cancer-Associated miRNAs in Saliva: First Steps to an Easily Accessible and Reliable Screening Tool. Biomolecules, 12(10). doi:10.3390/biom12101366.
- Luger, K./Mader, A. W./Richmond, R. K./Sargent, D. F./Richmond, T. J. (1997): Crystal structure of the nucleosome core particle at 2.8 A resolution. Nature, 389(6648), 251 – 260. doi:10.1038/38444.
- Malathi, N./Mythili, S./Vasanthi, H. R. (2014): Salivary Diagnostics: A Brief Review. Hindawi Publishing Corporation ISRN Dentistry, 2014, 2-9.
- Zeitschrift für die gesamte Versicherungswissenschaft, 114 (2025) 3

- Martinez, S. R./Gay, M. S./Zhang, L. (2015): Epigenetic mechanisms in heart development and disease. Drug Discov Today, 20(7), 799-811. doi:10.1016/j.drudis. 2014.12.018.
- Mittal, S./Bansal, V./Garg, S./Atreja, G./Bansal, S. (2010): The diagnostic role of saliva A Review. Journal of Clinical and Experimental Dentistry, e314-e320. doi:10.4317/jced.3.e314.
- Moutinho, C./Esteller, M. (2017): MicroRNAs and Epigenetics. Adv Cancer Res, 135, 189-220. doi:10.1016/bs.acr.2017.06.003.
- NHGR Institute. (Ed.) (2023): Bethesda, Maryland, USA.
- Nodine, T. (2024): Revolutionizing Life and Health Insurance with epigenetic testing. USA: Kcik & Co Synergy Ltd.
- Palmer, D. E. (2007): Insurance, Risk Assessment and Fairness: An Ethical Analysis. In: Flanagan, P./Primeaux, P./Ferguson, W. (Eds.), Insurance Ethics for a More Ethical World, Vol. 7, 113 126. Emerald Group Publishing Limited.
- Pfaffe, T./Cooper-White, J./Beyerlein, P./Kostner, K./Punyadeera, C. (2011): Diagnostic potential of saliva: Current state and future applications. Clinical chemistry, 57(5), 675 687. doi:10.1373/clinchem.2010.153767.
- Pigeyre, M./Yazdi, F. T./Kaur, Y./Meyre, D. (2016): Recent progress in genetics, epigenetics and metagenomics unveils the pathophysiology of human obesity. Clin Sci (Lond), 130(12), 943 986. doi:10.1042/CS20160136.
- Poussin, C./Titz, B./Xiang, Y./Baglia, L./Berg, R./Bornand, D./... Peitsch, M. C. (2024): Blood and urine multi-omics analysis of the impact of e-vaping, smoking, and cessation: from exposome to molecular responses. Sci Rep, 14(1), 4286. doi:10.1038/s41598-024-54474-2.
- Sailani, M. R./Halling, J. F./Moller, H. D./Lee, H./Plomgaard, P./Pilegaard, H./... Regenberg, B. (2019): Lifelong physical activity is associated with promoter hypomethylation of genes involved in metabolism, myogenesis, contractile properties and oxidative stress resistance in aged human skeletal muscle. Sci Rep, 9(1), 3272. doi:10.1038/s41598-018-37895-8.
- Saldanha, K./Staehle, T. (2023): Seeing the people behind the policies. Retrieved from Dublin: https://www.accenture.com/content/dam/accenture/final/industry/insurance/ document/Accenture-Insurance-Consumer-Study-People-Before-Policies.pdf#zoom= 40.
- Schuol, R./Rockoff, S./Ranisch, M. (2015): Selbstgestaltung des Menschen durch Biotechniken. Tübingen: Francke Verlag.
- Seaborne, R. A./Strauss, J./Cocks, M./Shepherd, S./O'Brien, T. D./van Someren, K. A./... Sharples, A. P. (2018): Human Skeletal Muscle Possesses an Epigenetic Memory of Hypertrophy. Sci Rep, 8(1), 1898. doi:10.1038/s41598-018-20287-3.
- Smith, J. A./Kohn, T. A./Chetty, A. K./Ojuka, E. O. (2008): CaMK activation during exercise is required for histone hyperacetylation and MEF2A binding at the MEF2 site on the Glut4 gene. Am J Physiol Endocrinol Metab, 295(3), E698-704. doi:10.1152/ajpen do.00747.2007.

- Stiftung Gesundheitswissen. (2022): Immer mehr Menschen mit chronischen Erkrankungen über Jahrzehnte beeinträchtigt [Press release]. Retrieved from https://www.stiftung-gesundheitswissen.de/presse/immer-mehr-menschen-mit-chronischen-erkrankungen-ueber-jahrzehnte-beeintraechtigt.
- Stirling, J. (2024): Insurance Collaboration to Save Lives. Retrieved from https://www.insurancecollaborationtosavelives.org.
- Terruzzi, I./Senesi, P./Montesano, A./La Torre, A./Alberti, G./Benedini, S./... Luzi, L. (2011): Genetic polymorphisms of the enzymes involved in DNA methylation and synthesis in elite athletes. Physiol Genomics, 43(16), 965–973. doi:10.1152/physi olgenomics.00040.2010.
- *Tollefsbol*, T. O. (2023): Handbook of epigenetics: The new molecular and medical genetics. Third edition. ed., London, United Kingdom; San Diego, CA: Academic Press, an imprint of Elseiver.
- Van den Ackerveken, P./Lobbens, A./Turatsinze, J. V./Solis-Mezarino, V./Volker-Albert, M./ Imhof, A./Herzog, M. (2021): A novel proteomics approach to epigenetic profiling of circulating nucleosomes. Sci Rep, 11(1), 7256. doi:10.1038/s41598-021-86630-3.
- Vehmeijer, F. O. L./Kupers, L. K./Sharp, G. C./Salas, L. A./Lent, S./Jima, D. D./... Felix, J. F. (2020): DNA methylation and body mass index from birth to adolescence: meta-analyses of epigenome-wide association studies. Genome Med, 12(1), 105. doi:10.1186/s13073-020-00810-w.
- Volk, N./Paul, E. D./Haramati, S./Eitan, C./Fields, B. K. K./Zwang, R./... Chen, A. (2014): MicroRNA-19b associates with Ago2 in the amygdala following chronic stress and regulates the adrenergic receptor beta 1. J Neurosci, 34(45), 15070 – 15082. doi:10.1523/JNEUROSCI.0855-14.2014.
- Wegwarth, O./Pashayan, N./Widschwendter, M./Rebitschek, F. G. (2019): Women's perception, attitudes, and intended behavior towards predictive epigenetic risk testing for female cancers in 5 European countries: a cross-sectional online survey. BMC Public Health, 19(1), 667. doi:10.1186/s12889-019-6994-8.
- Weis, S. (2024): Wie Beschwerdeprävention in der Lebensversicherung aussieht. Retrieved from https://www.versicherungsbote.de/id/4930788/Wie-Beschwerdepravention-in-der-Lebensversicherung-aussieht/.
- Wrzesniak, M./Kepinska, M./Krolik, M./Milnerowicz, H. (2016): The Influence of Tobacco Smoke on Protein and Metal Levels in the Serum of Women during Pregnancy. PLoS One, 11(8), e0161342. doi:10.1371/journal.pone.0161342.
- Wu, F./Yin, R. (2022): Recent progress in epigenetics of obesity. Diabetol Metab Syndr, 14(171). doi:https://doi.org/10.1186/s13098-022-00947-1.