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Roadmap
Chemistry of Life

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ROADMAP CHEMISTRY OF LIFE

1. Introduction

Understanding of Life on a molecular level (Chemistry of Life) provides a key that unlocks unlimited opportunities for breakthrough innovations, needed to address our global challenges for people today, and generations to come. The unifying aim in Chemistry of Life is therefore to bring about the chemical means and molecular understanding leading to an improved, more precise, personalized and effective healthcare as well as more sustainable and healthy food for the benefit of mankind.

Life entails a complex collection of molecules that enable, regulate, improve or threaten life. During the past century, scientific breakthroughs in (bio)chemistry led to the identification of molecules which are building blocks of life. We increasingly understand their functions, how they interact with small molecules and how they contribute to life. The fundamental understanding of the building blocks of life is applied in industries to develop products, improving life for individuals and society as a whole. While progress is enormous, leading to novel and targeted medicine and securing our food supply for a growing population, we still face major gaps in our understanding of life on a molecular level. At the same time, we are confronted with great challenges in healthcare as well as a sustainable healthy food supply.

What are the next scientific breakthroughs in Chemistry of Life? How can the Netherlands contribute to these by using and further developing our excellent knowledge infrastructure and network of world class universities, knowledge institutes and the private sector? How can we capture innovations and economic growth in The Netherlands based on these breakthroughs (e.g. through our world-class food production systems and by expanding current vibrant biotech start-ups and establish novel ventures)?

The answers will come from **collaborations**. Collaborations across disciplines, across industries (value chains), and across the world. The Chemistry of Life roadmap therefore has a focus on chemistry and molecular insights that will be embedded in all sectors that contribute to the scientific and economic breakthroughs the top sector Chemistry wishes to enable. These connections are further specified in section 4.

A three-pillar (task) roadmap has been developed to address the scientific challenges and economic opportunities in healthcare (task 1) and food/nutrition (task 2) and the link between them, connecting health and food/nutrition (task 3).

The **first pillar** (task 1) focuses on ‘Molecular entities, devices and approaches for understanding, monitoring and improving **precision healthcare**’.

Many human diseases are the result of altered or malfunctioning molecular/cellular mechanisms and genetic mutations. Detailed understanding of cellular wiring in the normal and, by contrast, the diseased states is essential to develop (therapeutic) approaches that prevent diseases, or re-program and revert cells to a normal healthy state or trigger cell death (apoptosis) to eliminate defective cells. Genomics, transcriptomics, proteomics, metabolomics data (omics) obtained using advanced (clinical) analyses of patient material constitute a treasure trove to understand and redirect molecular pathways. Fundamental disciplines including molecular biology, biochemistry and medicinal chemistry together define the relevant interactions and events disturbed in disease and targeted in therapy. Emerging infectious diseases and antibiotic resistance are urgent health threats that can only be addressed with new chemical insights and knowledge and its applications. The identified health(care) related chemical processes can then be targeted by existing or newly developed drugs with more precise and efficient effect. Thus contributing to the KIA Health & Care with the mission that by 2040, all Dutch citizens will live at least five years longer in good health.

The **second pillar** (task 2) focuses on ‘Molecular entities, technologies and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious, delicious food and feed to optimize health and wellbeing’. The Netherlands is leading in the application of technological solutions to food production and food security with for example Unilever, DSM and Danone Nutricia as key industrial parties located in the Netherlands. Chemistry is an essential element in food innovation. Chemistry will also enable the food sector to get to the next level in answering fundamental scientific questions to provide breakthrough innovations that address societal needs related to food quality and security throughout the whole lifespan. Sustainable food production and an increased contribution of renewable (plant-based) food to the human diet require new insights and understanding of food at the molecular level. This way, (bio)chemistry supports the missions formulated in the KIA Circular Economy which also aims for optimal use of resources, including biological resources and manufacturing processes. In addition, it is crucial to understand which molecules are present, the exact location and understand how these molecules mutually interact and build the supramolecular systems in foods responsible for flavour and taste as well as nutritional features and bioavailability of food nutrients.

The **third pillar** (task 3) focuses on **enabling technologies** and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life. This pillar creates a deeper **understanding of the building blocks of life** and developing **enabling technologies** while providing valuable input for understanding, monitoring and improving health(care), food security and eventually other sectors such as bio-inspired materials, circular economy and sustainable energy. Thus contributing to the KIA Health & Care with the mission that by 2040, all Dutch citizens will live at least five years longer in good health.

	Short term **Now-2022**	**Mid term** **Now-2030**	**Long term** **2030-2040**	**Programme Line ambition**
Molecular entities, devices and approaches for understanding, monitoring and improving precision healthcare	- Personalized omics analysis - Drug development for orphan diseases - Understanding material properties contributing to improved compatibility with human bodies and cells.	- Target identification for (multifactorial) diseases - Multidisciplinary multi-centre of Drug Discovery (e.g. Future Medicine Initiative) which enforces the cluster Chemical technologies in the KIA Key Technologies - Structural information on the interaction of NCEs and bio-conjugates with target proteins - Explore new functionalities of Materials in human bodies (e.g. stability, release, mechanical strength, lubrication, antimicrobial, molecular detection and reporting) which enforces the cluster Advanced Materials in the KIA Key Technologies	- Development of novel clinically affordable disease- oriented workflows and devices directly enforcing Mission II Access to Healthcare (KIA Health & Care) - Development of New Chemical Entities (NCEs), biopharmaceuticals and bio- conjugates for use in diagnostics, in vivo imaging, and clinical applications - Piloting and commercialization of new materials and devices	*Improved and more affordable precision healthcare*
Molecular entities, technologies and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious, delicious food and feed to optimize health(care) and wellbeing	- Molecular understanding of factors impacting texture/taste - Validated biomarkers of nutritional status in order to progress from descriptive models to predictive models - Development of products that improve nutritional status and optimization of guidelines and dietary	- Novel enzymes/microbes that tailor texture/taste both *in-situ* and *ex-situ* - Quantitative and mechanistic models of in vitro and in vivo digestion of foods based on biochemical properties of food constituents - Novel biochemical processes for obtaining ingredients with reduced	- New, biochemically derived health promoting substances, including enzymes and micro-organisms with a link to life science technologies: ST7-4 Gene Editing / Precise Genetic Engineering - Correlation of in vitro and in vivo digestion models: what happens during digestion in humans	*Improved and more sustainable food*

	recommendations - Identification of new, optimal chemical processing of new, sustainable sources for protein supply which enforces the KIA Circular Economy; MMIP2AQ3 - Adapt feeds to reduce nitrogen, phosphate and/or sulphur emission which enforces the KIA Circular Economy; MMIP2AQ11.	environmental footprint - Molecular localization methods including spatially and time resolved analysis tools for food ingredients and finished products	and full functionality of whole GI tract including taste and texture - Novel ingredients to replace current, undesired food additives that are used to reduce spoilage supporting the missions formulated in the KIA LWV and the KIA CE.	
Enabling technologies and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life	- Insight into the impact of the heterogeneity of proteins and protein complexes on cellular networks - Building Blocks of Life, 16 projects that are currently running, supported by TKI Chemistry together with other topsectors which support the missions formulated in the KIA LWV and the KIA Health & Care and enforces the cluster Life Science Technologies in the KIA Key Technologies - Novel biocatalytic enzymes carrying out unique chemistries	- Influence of heterogeneity in the dynamics of bio molecular networks and on the robustness of systems - Minimal cells that conduct specific biochemical reactions and biotransformations in a robust manner and that can be used in industrial applications related to bioenergy, biomaterials, chemical production - Markers for food quality and spoilage and food borne pathogens supporting the missions formulated in the KIA LWV and the KIA CE.	- Utilize the knowledge on network dynamics and cellular heterogeneity to tackle challenges in energy, food and health(care). - Synthetic cell-like entities (eukaryotic and prokaryotic) that in a controlled manner carry out complex coupled processes including basic biochemical reactions that can replicate - "Organ-on-a-Chip" modules that can be used as a disease specific screening	*Accurate cell systems for medical, food and energy applications*

Table 1

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ChemistryNL Roadmap	Energy Transition and Sustainability			Agriculture, water and food	Health and Healthcare	Security	Key Technologies	Societal earning capacity
	Climate and Energy (IKIA) *in particular Mission C "Industry"*	Circular Economy	Future Mobilitysystems	7 missions	4 missions	8 missions	Key technnology (ST) clusters: ChemTech, AdvMat, DigTech, EngFabTech, LifesciTech, NanoTech, PhotoTech, QanTech	3 tracks
Chemistry of Life							LifeSciTech, ChemTech	
Molecular entities, devices and approaches for precision healthcare		(Bio)chemistry supports the missions formulated in the KIA Circular Economy which also aims for optimal use of resources, including biological resources and manufacturing processes.			Wearable diagnostic devices eliminate the need for visiting the hospital, are instrumental to avoid clearly dangerous environmental chemical entities or enable to remove these from environment (smart filters/absorbers) and prevent disease and directly enforces Mission II, access to healthcare of the KIA Health & Care		Creation of new chemical, molecular, biological and cellular entities to interact with and predictably modify chemical properties of biomolecules for treatment and the exploration of new functionalities of Materials in human bodies enforces the cluster Advanced Materials in the KIA Key Technologies ; New, biochemically derived health promoting substances, including enzymes and micro- organisms link to life science technologies: ST7-4 Gene Editing / Precise Genetic Engineering	
technologies and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious delicious food and		Biochemical tailoring of food, Sustainable production, longer shelf life of food products and new sources of e.g. proteins and the development of novel ingredients to replace current, undesired food additives that are used to reduce spoilage supporting the missions formulated in Mission CE (MMIP2AQ3) and also the adaptation of feeds to reduce nitrogen, phosphate and/or		Biochemical tailoring of food, Sustainable production, longer shelf life of food products and new sources of e.g. proteins and the development of novel ingredients to replace current, undesired food additives that are used to reduce spoilage supporting the missions formulated in the KIA LWV; Mission B & D			To improve food quality in terms of texture/flavour (sensoric experiences) and health related issues, foods can be tailored by physical as well as (bio)chemical ways. With advances in biochemistry and compositional combined with computational analysis (including chemometrics approaches), additional means became available to understand and modify foods and/or ingredients in a precise and also more sustainable way. Such developments are of crucial importance in the transition away from animal-based protein supplies towards more environmentally friendly plant-based protein sources with their associated reduction of greenhouse gas emissions and enforces the cluster Life Science Technologies in the KIA Key Technologies.	
Enabling technologies and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life		Designer minimal cells for application and production in bioenergy, biomaterial and (bio-)chemical production and Markers for food quality and spoilage and food borne pathogens support mission CE		Designer minimal cells for application and production in bioenergy, biomaterial and (bio-)chemical production and Markers for food quality and spoilage and food borne pathogens and Building Blocks of Life projects support the missions formulated in the KIA LWV; Mission B &D	Building Blocks of Life support the missions formulated in the KIA Health and Healthcare; Mission I, II and III; The chemical knowledge generated for diagnostics and the information on the chemical status in a body contributes to the KIA Health & Care, mission I (lifestyle and environment) and mission III (chronic diseases). Cell like entities as smart diagnostic and therapeutic agents contribute to the improvement of health and healthcare, the overall aim of the KIA Health & Care.		Building Blocks of Life support and make use of Key Technologies; Designer minimal cells for application and production in bioenergy, biomaterial and (bio-)chemical production support the cluster Advanced Materials in the KIA Key Technologies; Tailor made platforms for high throughput drug screening.	

2. Collection of tasks

A unifying aim in the Chemistry of Life theme is to bring about the chemical means that facilitate improved and more affordable precision healthcare and more sustainable and healthy food, both benefitting the future of mankind.

2.1. **Task 1**: Molecular entities, devices and approaches for understanding, monitoring and improving precision healthcare are relevant for e.g. cancer diagnosis, prognosis and treatment. Insight into specific molecular defects and targeting of these targeted strategies appear effective, but not all molecular defects developed as treatment targets can overcome treatment failure and recurrence. More detailed understanding of the complex responses based on understanding of the integrated chemical network of cells is key. This is equally relevant for other chronic diseases of tissue degeneration (neurodegeneration, circulatory system, joints) where chemical clues can be used as early warning and chemical intervention needs to be designed to reach the specific sites involved and have the desired regenerative effect. This task directly supports mission III of the KIA Health & Care (chronic diseases).

2.1.1 Development of analytical and biophysical devices (e.g. chemical read out on biopsy samples, molecular imaging for non-invasive imaging applications, computational tools for -omics analysis of complex traits) which enforces Mission II Access to Healthcare (KIA Health & Care)

2.1.2 Creation of new chemical, molecular, biological and cellular entities to interact with and predictably modify chemical properties of biomolecules for treatment (e.g. eliminate cancer cells, restore neuronal function, repair degenerated joint tissue, kill microbes and virus infected cells, or prevent infection, stimulate immune responsiveness specifically to diseased cells, address orphan diseases). Explore new functionalities of materials in human bodies (e.g. stability, release, mechanical strength, lubrication, antimicrobial effect, molecular detection and reporting) which enforces the cluster Advanced Materials in the KIA Key Technologies

2.1.3 Biomedical materials for improved functionalities (with applications in transplantation, joint repair, to increase the longevity and function of *ex vivo* organoids or biopsies, enabling study and diagnosis, scaffold cells for tissue repair and delivery of therapeutic chemicals in a localized and controlled way) which enforces the cluster Advanced Materials in the KIA Key Technologies

2.1.4 Lifestyle & environment (wearable diagnostic devices eliminate the need to visit the hospital, are instrumental to avoid clearly dangerous environmental chemical entities or to remove these from environment (smart filters/absorbers) and prevent disease) and directly enforces Mission II of access to Healthcare (KIA Health & Care)

2.1.5 Sustainable production (devices and entities that biodegrade, are smaller and do not need to be disposed of and stimulate re-use in complex synthesis and production). This can be linked with the cluster Chemical technologies in the KIA Key Technologies.

2.2. **Task 2**: 'Molecular entities, technologies and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious, delicious food and feed to optimize health and wellbeing and to prevent noncommunicable (like cardiovascular disease, diabetes and cancers) and neurodegenerative diseases (like dementia). This task directly supports the central mission of the KIA Health & Care and specific missions III (chronic diseases) and IV (dementia).

2.2.1. Biochemical tailoring of food. The correlation between food composition, microbiome and disease allows for the tailoring of food to promote a beneficial health status and microbiome (in some cases disease-specific). Food and diet can also be tailored to promote a healthy immune system with the food being a source of therapeutic agents. For this all there is a strong need to know what nutritional components are crucial for maintaining and regaining health and preventing specific diseases. Altering the food chemical composition can also aid to make the food last longer and better maintain nutrients in storage and transport. Thus supporting the missions formulated in the KIA LWV and the KIA CE

2.2.2. Understanding food digestion and metabolism to increase nutritional availability and health. Correlate in vitro and in vivo digestion models to explain what happens during digestion in humans and full functionality of the whole GI tract including taste and texture

2.2.3. Sustainable production and consumption. Feeding the ever-increasing world population in a sustainable manner is becoming a true challenge which is also addressed in the KIA LWV and the KIA Circular Economy. Through this Chemistry of Life roadmap, new sources of e.g. proteins are currently being implemented. Consumer acceptance is modest due to flavour and taste defects caused by the presence of off-flavours generated in the growing of plants or in later food manufacturing and storage. Blocking (enzymatic) formation routes and other mitigation strategies require a detailed molecular understanding of (plant) cellular mechanisms.

2.3. **Task 3**: Enabling technologies and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life
- 2.3.1 Understanding of cellular processes from molecule to organism
- 2.3.2 Engineering of molecules and cells
- 2.3.3 Technologies to measure and track food deterioration and food borne pathogens

3.1 Task 1: Molecular entities, devices and approaches for understanding, monitoring and improving precision healthcare

In the Chemistry of Life Program first of all, **analytical and biophysical tools and methods** need to be further developed that assist us to monitor the molecular entities, not only in our body, but also in animals, plants, fungi and other organisms. In the future human, animals and plant, healthcare will only be more intertwined. For future healthcare such approaches will allow us to develop new diagnostics for early discovery and enable a more personalized and precise health care monitoring and disease prevention. This will enable one to monitor the status of healthy individuals, and of patients with chronic diseases and detect disease in more early stages. Impact of lifestyle, and environment on health can also be monitored by these means. Additionally, they will help to balance safety and efficacy in the nutrition chain.

Importantly, new molecular and cellular entities will be synthesized and/or designed, ranging from highly selective inhibitors to adapted cellular therapies (such as stem cells and gene therapies and tailor- made vaccines). This Task is related to the central mission of the KIA Health & Care and specific missions II (Access to healthcare) and III (chronic diseases).

3.1.1 Development of analytical, biophysical devices and cellular model systems

Most human diseases are the result of altered and/or malfunctioning of molecular and/or cellular mechanisms and genetic mutations. The molecular basis of disease is often poorly understood. Moreover, current therapies appear ineffective for some patients and drug resistance may occur. Quantitative patient-derived **omics analysis** and model-based predictions (using big data and artificial intelligence) constitute a treasure trove to understand which molecular pathways are affected and may be targeted by (existing) drugs, thus offering an avenue towards precision medicine.

To achieve this:

We need to explore and develop analytical and biophysical strategies and devices, cellular model systems and approaches for monitoring, understanding and target identification to improve more precise (personalized) and effective healthcare. Application of novel sensor systems also include low cost, non-invasive systems to monitor the nutritional status of cells and their response to food and nutritional ingredients. This is related to the KIA Key technologies, cluster Life science technologies Q2 (develop reliable implants that monitor and/or treat medical conditions) and Q3 (developing medical devices that monitor body parameters and medical conditions invisible on the skin or easily accessible at home or in primary care for preventive healthcare or the monitoring of chronic diseases) and chemical technologies ST1-2 Analytic Technologies Q2 (develop micro-analytical systems to measure cellular structures and body fluids in real-time with techniques for multiscale analysis of the local molecular processes and the related medical conditions).

Specific steps required present-2040:

I. Development of diagnostic workflow/devices:
- Establish large-scale multi-centre infrastructures for the quantitative analysis of all bio-molecular

entities such as the Future Medicine Initiative (genomics, proteomics, metabolomics, structural biology, bio-imaging, chemical biology etc.)

- Determine which biomolecular entities and combinations are relevant/robust to predict disease state, prognosis, treatment options and or treatment success
- Development of high-throughput novel diagnostic analytical workflows and devices for (multifactorial) diseases
- Translation into ultra-sensitive, easy-to-use, low-cost micro-devices useable in precision healthcare

II. Obtain novel insights into molecular mechanisms of disease

- Develop novel synthetic and cellular platforms/model systems (e.g. pluripotent stem cells (iPSCs) derived cells/organoids; 3D cellular co-cultures; multiplex high content imaging) and analytical tools for networked biochemical processes, diagnosis and intervention.
    - Identify sets of molecular components, interactions and complex signalling networks representative for disease state or response to treatment
- Network based analysis of diseases using chemo-/bioinformatics, pharmacogenomics and systems biology to understand the relationship between human physiology, the microbiome and the environment.
    - Identify critical and accessible steps in molecular pathways and networks for novel (multifactorial) intervention and targeting.

Milestones:

- Personalized omics analysis, relevant robust markers of disease process identified and validated
- Establishment personalized (iPSCs-based) (2/3D) multi-cellular model systems (cells/organoids)
- Target identification for (multifactorial) diseases
    - Enabled network-based analysis of disease based on quantitative profiling of patient material using chemo-/bioinformatics, pharmacogenomics and systems biology
    - Device (multi-) targeted therapies for (multifactorial) diseases
- Developed novel clinically affordable disease-oriented workflows and devices
    - New and affordable personalized diagnosis and care

Expected results present- 2040:

Scientific/technological goal: Target-based therapy established on disease network analysis.

Industrial end goal: Translation of diagnostic tools and analysis to commercialization.

Societal goal: Cohort of patients performing disease related self-diagnosis or self-monitoring thus contributing to Mission II (Access to Healthcare) of the KIA Health & Care

3.1.2 Creation of new chemical, molecular and cellular entities

Over the last decade, advances in genetic and proteomic analysis have led to the identification of a large set of genes/proteins that play a key role in disease. It is an enormous challenge to determine which of these genes/proteins are suitable drug targets. These **target genes and proteins** need to be studied on a molecular level and their activities perturbed with small-molecule compounds, biologicals or genetics to validate them as *'druggable'*. This offers enormous opportunities for the Netherlands and especially for chemistry in the life sciences field. Chemistry is key in the development of novel assay technologies, diagnostic agents and it provides the starting point for the development of **novel classes of drugs** in areas of unmet needs. An investment in target validation on a molecular level, small molecule screening, medicinal chemistry or antibody-based approaches will allow the development of small molecule drugs/biologicals that allow more effective and affordable treatment of disease.

To achieve this:

In order to translate current genetic and proteomic knowhow into novel therapies, several steps need to be taken including strengthening of specific expertise and infrastructure establishment. Examples of opportunities for drug development include novel drugs/biologicals that can be used to treat cancer, infectious-, metabolic-, auto-immune-, and genetic diseases as well as medication that acts on the central nervous system and drugs that aid tissue regeneration. Likewise, opportunities exist for the development of biologicals and cell-based therapies and creation of new chemical, molecular and cellular entities. Novel chemical probes and assays need to be developed for detailed studies of targets on a molecular level. Simultaneously such probes may aid the development of diagnostic agents.

Specific steps required present-2040:

I. Assay development for selection of bioactive (bio)molecular entities:

- Development of novel miniaturized assay formats for High Througput Screening (HTS) and fragment-based approaches (e.g. FRET, fluorescence polarization, activity-based profiling) for identification of well-defined target selective new chemical entities (NCEs) and biologicals.
- Validation of assays for high content screens and cell-based assays for identification of well-defined target selective NCEs and biologicals.
- Development of target or class specific probes for studies of drug action in cells and animal models. These probes also offer opportunities for the development of diagnostic and imaging agents.

II. Design and synthesis of new (bio)molecular entities which enforces the cluster Chemical technologies in the KIA Key Technologies :

- Synthesis and biochemical programs aimed at the development of bioactive molecules that can serve as therapeutic agents. Further characterization of novel (bio)chemical entities, and the cellular processes and networks they act on.
- Precision medicine. Development and application of tailor-made NCEs and biologicals aimed at (families of) disease-related targets (for unmet disease areas).
  - Development of first tool compounds/biologicals, which are entities that validate molecular targets for the treatment of specific diseases.
  - Development of candidate drugs that act on targets validated with tool compounds.
  - Development of matching probes that can be developed into imaging and diagnostic agents.
- Structure-based drug design (SBDD)
  - Obtain structural information of target protein to develop 3D molecular models of targets.
  - Binding mode prediction and (virtual) screening for selection of candidate molecules.
  - Parallel high throughput crystallography and structure determination.
  - Design and optimization of molecular entities.

Milestones:

- Development of NCEs, biologicals and bio-conjugates for use in diagnostics, in vivo imaging, and clinical applications.
  - Omics data exploited by the development of novel tool compounds and matching diagnostic probes.

- Proof of Concept realized for several NCEs, biologicals in Phase 1 and phase 2 clinical trials.

- Structural information on the interaction of NCEs, biologicals and bio-conjugates with target proteins available

- Multidisciplinary multi-centre of Drug Discovery:
  - Establishment of a centralized infrastructure to prepare, store, analyse, model and test Dutch collections of small molecules and bioactive compounds for HTS and high content screening purposes.
    - Compound logistics
    - IP issues (or open source innovation plan)
    - Outreach to partners with relevant targets
  - Further development of drug candidates and biologicals into new affordable medicines and affordable entities for diagnosis and therapy.
    - Coordinated small molecule synthesis, medicinal chemistry, chemical biology based approaches and central screening and characterisation both in vitro and cell- based and high content.
    - Public-private partnerships for further development of NCEs.

<u>Expected result present- 2040:</u>

Scientific/technological goal: development (bio)molecular entities for diagnostic and therapeutic applications. This will require a Dutch multidisciplinary centre for Drug Discovery providing HTS services and high content screening.

Industrial end goal: New diagnostic probes, high quality NCEs, biologicals for further development towards marketed drugs that serve unmet medical areas. Establishment of novel ventures.

Societal goal: New diagnostics and new drugs leading to, healthier living, and better health(care), and better understanding and control of disease by affordable small molecules or biologicals thus contributing to the KIA Health & Care.

3.1.3 **Biomedical Materials for improved functionalities,** which enforces the cluster Advanced Materials in the KIA Key Technologies

Development of improved biomedical materials to reduce the burden for a variety of diseases offers an important solution to unceasingly rising healthcare costs and requirements for a better quality of life. Biomedical materials can improve the performance of for instance implants, medical devices, scaffolds and drug delivery systems. Furthermore, superior biomedical materials may help minimize side-effects and the need for invasive surgery.

<u>To achieve this:</u>

In order to generate novel and improved biomedical materials for safe, cheap and widespread use in surgery and monitoring of disease, several phases of the innovation pipeline need to be strongly connected. Aspects of fundamental chemical research for improved functionalities, production processes and medical evaluation for in vivo use are to be jointly tackled. Examples of application areas for improved biomedical materials include in vivo sensors, cardiovascular surgery, oncology, muscoskeletal, nephrology, drug delivery systems and implants. This is related to the KIA Key technologies, cluster Life science technologies Q2 (develop reliable implants that monitor and/or treat medical conditions) and Q3 (developing medical devices that monitor body parameters and medical conditions invisible on the skin or easily accessible at home or in primary care for preventive healthcare or the monitoring of chronic diseases) and chemical technologies ST1-2 Analytic Technologies Q2 (develop micro-analytical systems to measure cellular structures and body fluids in real-time with techniques for multiscale analysis of the local molecular processes and the related medical conditions).

<u>Specific steps required present-2040:</u>

I. Understanding material properties contributing to improved compatibility in human cells.

II. Explore new functionalities of Materials in human bodies (e.g. stability, release, mechanical strength, lubrication and antimicrobial).

III. Development of new materials and devices.

IV. Piloting and commercialization of new materials and devices.

Milestones:

- New insights in basic principles created
- proof of principles established

Expected result present- 2040:

Scientific/technological goal: New leads for Biomedical Materials developments established, Dutch centres of excellence and international network established (PPPs).

Industrial end goal: High quality biomedical materials with wide array of application areas and large market potential in medical interventions.

Societal goal: improved health care due to improved quality of life, reduced side effects or need for invasive surgery thus contributing to the KIA Health & Care.

Examples of MJPs related to this pillar:

MJP02 Building Blocks of Life Begrip en benutting van cellulaire sytemen

MJP13 Smart personalized food and medicine

MJP16 MedTech

MJP17 Biomedical Engineering for Health

MJP71 Meet- en Detectietechnologie

MJP72 Evidence Based Sensing

MJP86 Bridge – Life Science Technologies

MJP87 Vitality, Lifestyle and Ageing-in-place for people with (early) dementia

Examples of initiatives related to this task:

Gravity Programs such as Institute of Chemical Immunology and Cancer GenomiCs.nl, Roadmap Infrastructure Proteins@Work and uNMR.nl, TI-COAST, Pivot Park Oss, European Innovative Medicines Initiative (IMI), FIGON, Roadmap NL-BioImaging AM, DTL, OneHealth and CeSAM.

3.2 Molecular entities, technologies, devices and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious, delicious food and feed to optimize health and wellbeing

3.2.1 Biochemical tailoring of food

Consumers have increasing demands for the quality of their food. To improve food quality in terms of texture/flavour (sensoric experiences) and health related issues, foods can be tailored by physical as well as (bio)chemical ways. With advances in biochemistry and compositional combined with computational analysis (including chemometrics approaches), additional means became available to understand and modify foods and/or ingredients in a precise and also more sustainable way. Such developments are of crucial importance in the transition away from animal-based protein supplies towards more environmentally friendly plant-based protein sources with their associated reduction of greenhouse gas emissions and support the missions formulated in the KIA LWV and the KIA CE and enforces the cluster Life Science Technologies in the KIA Key Technologies. (Biochemical) Tailoring exploiting the versatility of food and food ingredients with optimal processing, flavour and texture will allow us to turn plants into tasty, safe and nutritious foods.

To achieve this:

Biochemical tailoring of food and food ingredients (including live/viable cultures) should include:

a. Understanding the production routes of (off-) flavour and taste compounds in plants and methods to modify these.
b. Enzymatic or microbial production of flavour, texture and health supporting substances.
c. Molecular understanding of the food matrix and ingredient (enzymes, microbes) interaction leading to a desired food performance.
d. Correlate *in vitro* and *in vivo* digestion models to explain what happens during digestion in humans and decipher the full functionality of the whole GI tract including taste and texture sensing

Specific steps required present-2040:

Short term:

I. Identify relevant flavour forming reactions in foods and fermented foods that can or have to be improved, both in situ in foods and ex-situ productions of flavours
II. Identify specific locations of molecules, quantify intermolecular interactions in foods and understand how molecules build multiscale structural organisations affecting protein binding, the uptake of nutrients and the experience of flavours
III. Identify suitable health promoting substances that are formed by a limited number of enzymatic reactions, using microbes or that are plant derived.
IV. Advancing sensory science (texture, taste/flavour combination).

Long term:

V. Produce and apply enzymes or microbes to improve or stabilize flavour in foods and/or ingredients.
VI. Enhanced production of taste, nutrition and health promoting substances within the food matrix.
VII. Cascading enzyme reactions including activation of desired nutrient formation routes and inactivation of formation routes of off-flavours or natural toxins or anti-nutrients.
VIII. Connecting sensory science (incl. texture/taste combination) with molecular understanding to guide food tailoring.

Milestones:

- Insight in and control of formation routes of off-flavours, toxins and anti-nutrients in plant-based materials
- Improved nutrient delivery through controlling protein/small molecule interaction
- Molecular understanding of factors impacting texture/taste.
- Novel enzymes/microbes that tailor texture/taste both in situ and ex-situ.
- New, biochemically derived health promoting substances, including enzymes and micro-organisms.

<u>Expected result present- 2040:</u>

Scientific/technological goal: Improved insight in biochemistry of processes occurring during food and food ingredient production.
Industrial end goal: more controlled tasty and healthy food, personalized food. Increased flexibility in terms of raw materials.

Societal goal: Longer shelf life of food products and less waste due to too low flavour or off-flavour formation. All food produced in a circular manner with limited environmental impact. Thus supporting the missions formulated in the KIA LWV and the KIA CE.

3.2.2 Understanding food digestion and metabolism to increase nutritional availability and health

An important mission to improve the value of food is increased nutritional availability and contribution to health. Modern urban populations suffer from the so called “triple burden” of malnutrition, by which the coexistence of hunger, nutrient deficiencies, and excess intake of calories leading to overweight and obesity create a serious threat to human health. Increased nutritional availability and improved health status by (bio)chemical advances and improved understanding of nutrition and health will greatly reduce this health threat.

<u>To achieve this:</u>

Increased efficiency of use of foods by increased nutritional availability of food constituents is needed. Key to this is the understanding of the molecular processes and interactions taking place during the digestion of foods, including the role of the gut microbiota. More specifically, this includes:

a. Identifying biomarkers of pre- and probiotics
b. Nutritional value: Understanding digestion kinetics (*in vitro* and *in vivo*).
    - Understanding of enzymatic/fermentation kinetics relevant for the food bolus; Enzymology of “Crowded system dynamics”.
    - Understanding molecular interactions during digestion/fermentation processes.
c. Dynamic effects of metabolized food components (host, microbiota and interplay between the two) on tissue and organ functions (e.g. brain, muscle, immune system, gut).
    - Engineering of food to target specific organs or cells.

<u>Specific steps required present-2040:</u>

Short term

I. Establishment of mechanistic molecular descriptors of hydrolysis/fermentation kinetics of food constituents.
II. Establishment of physico-chemical descriptors of hydrolysis/fermentation processes of food constituents in semi-solids systems.

Quantitative correlations between the microbiota composition and the occurrence and/or formation of prebiotics during intestinal fermentation.

Long term

III. Integration of molecular and physico-chemical parameters to describe the spatial and temporal resolution of food digestion/fermentation products in the digestive tract during consumption of foods for healthy and diseased individuals of different ages (from new-borns to elderly).

Milestones

- Validated biomarkers of health and disease in order to come from descriptive models to predictive models.
- Quantitative and mechanistic models of *in vitro* and *in vivo* digestion of foods based on biochemical properties of food constituents.
- Correlation of in vitro and in vivo models.

Expected result present- 2040:

Scientific goal: Improve insight in connection between nutrition and health by understanding digestion.

Industrial end goal: Foods with optimal nutritional value and related added value.

Societal goal: Foods with directed impact the (bio)chemistry of health and disease. Thus supporting the central mission of the KIA Health & Care.

3.2.3 Sustainable production and consumption

Accelerated globalization and raised living standards leading to increased production and consumption of food are progressively threatening our climate, deplete natural resources and have a negative environmental impact. Responsible food production and consumption is a crucial aspect of improved food security and availability. Hence, there is a need for the creation of an “efficiency revolution” in the use of agricultural raw materials by making consumer preferred products based on plant materials, developing new technologies for making conversions more efficient and by preventing wastes and nutrient losses without the use of undesired chemicals. A biochemical approach is key to this development, thereby improving the sustainability of food supply. Knowledge of the chemistry and the molecules involved again is crucial.

This enforces the cluster Chemical technologies in the KIA Key Technologies; Q5 to develop cheap ad efficient electrochemical processes for the conversion of H20, CO2, N2 or biomass to fuels and raw materials for the chemical industry explicitly including the required scaling of these processes to GW level in the design and ST1-1 (Bio) process Technology Q1 Develop sustainable and effective conversion of biomass to raw materials and specialty chemicals through micro-organisms for example for waste water conversion

To achieve this:

Food manufacturing should be carried out in a more sustainable manner than today. Important areas of attention to be elaborated on in this aspect relate to:

a. More sustainable food and food ingredient processing by less use of chemicals, water and energy (low temperature processing).
  - Food processes in concentrated and/or crowded systems.
  - Replacing “chemical” extraction of ingredients by aqueous (enzymatic) processes with full recycling of extractants and processing aids.

b. Understanding biochemical properties of terrestrial, aquatic or other raw materials for replacement of animal based foods/food ingredients (e.g. proteins).
  - Less spoilage of foods by exploring biochemical production and use of new nature inspired preservatives, e.g. lipid stabilizers, anti-oxidants, phenolics and microbial preservatives supporting the missions formulated in the KIA LWV and the KIA CE.

Specific steps required present-2040:

Short term

I. Development/adaptation of analytical methods to be used in concentrated and/or crowded systems.

II. Understanding at a molecular level the contributions of individual components within complex ingredients as well as isolated ingredients from existing and novel sources.
III. Understanding the fate of molecules in novel milder food processing methods.
IV. Identification of critical descriptors of enzyme function (selectivity, activity, stability, etc.) in concentrated/crowded systems.
V. Identification of highly selective and effective enzymes to release ingredients and/or to produce ingredients from raw materials.
VI. Control of biochemical conversion reactions deteriorating the properties of ingredients obtained from novel sources.

Long term

VII. Understanding functionality of food ingredients, (e.g. proteins) from a molecular perspective, taking into account also intermolecular interactions, thereby enabling implementation of existing and new food sources.
VIII. Targeted modification of food ingredients from existing and novel sources to enhance functionality and use.
IX. Establishment of mild-chemical, enzymatic or microbial routes to produce ingredients.

Milestones:

- Identification of new, sustainable sources for protein supply including methodologies to convert these into safe and nutritious, consumer-preferred products.
- Novel biochemical processes for obtaining ingredients with reduced environmental footprints.
- Mild processing routes retaining all positive nutrients while preserving quality and safety of the food.

- Novel ingredients to replace current, undesired food additives that are used to reduce spoilage by natural alternatives.

Expected result present- 2040:

Scientific goal: Understanding biochemical conversions in complex matrices and concentrated systems. Understanding biochemical production routes for new antimicrobials.

Industrial end goal: Improved sustainability of food production and consumption.

Societal goal: More efficient use of food and food ingredients to address food security and environmental burden. Thus supporting the missions formulated in the KIA LWV and the KIA CE

Examples of MJPs related to this pillar:

MJP04 High Tech to Feed the World

MJP06 Verbetering van de fotosynthese-efficientie

MJP13 Smart personalized food and medicine

MJP87 Vitality, Lifestyle and Ageing-in-place for people with (early) dementia

Examples of MMIPs related to this pillar:

MMIP2A Q11: stikstof en fosfaat

MMIP2A Q3: eiwittransitie

MMIP2A Q7: voedselverspilling

Examples of initiatives related to this task:

Carbohydrate Competence Center (CCC), multiple programmes within WageningenUR Food and Biobased Research, JPI a Healthy Diet for a Healthy Life, Top Institute Food and Nutrition (TIFN).

3.3. Enabling technologies and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life

This links to all Life Science technologies of the KIA Key Technologies and the cluster chemical technologies ST1-1 (Bio)Process Technology Q1: Develop sustainable and effective conversion of biomass to raw materials and specialty chemicals through micro-organisms for example for waste water conversion and to ST1-2 Analytic Technologies Q2: develop micro-analytical systems to measure cellular structures and body fluids in real-time with techniques for multiscale analysis of the local molecular processes and the related medical conditions.

3.3.1 Understanding of cellular processes from molecule to organism

Living cells are biochemical reaction factories. Many of the basic elements of enzymatic reactions have been studied in detail for isolated systems but how these integrate in large networks is still mysterious. We aim to understand how biochemical reactions occur in living cells. To advance on these challenges, a basic understanding of cellular systems at the molecular level is required, in particular with respect to functional heterogeneity among individual cells and the dynamics of complex networks. With this knowledge we aim to: engineer cells and cell like entities such that they fulfil specific tasks, use the molecular parts of cells to create new materials or even build designer cells, and build a synthetic cell from individual parts.

To achieve this:

The cell with all of its constituents forms the basic element of life. Our knowledge on these systems provides the foundation for advanced applications ranging from medicine and health, food, energy and materials. This task is focused on a fundamental understanding of the molecular structures, dynamics and interactions that define biological functions of individual living cells, including interactions with the environment and the heterogeneity within cell populations.

Specific steps required present-2040:

I. Understanding of complex cellular networks with an emphasis on dynamics.

Use of advanced methods in molecular imaging, ribosomal profiling and mass spectrometry to map cellular networks and their dynamics, and employ molecular biology, optobiology and chemical biology to perturb network processes and identify relevant physiological response.

II. Modelling of the network dynamics to allow for the accurate prediction of the behaviour of sub-cellular processes, cells and tissues under defined conditions taking heterogeneity into account.

III. Quantitative description of biochemical processes in individual cells.
  - Elucidate the molecular basis of cellular heterogeneity by large scale imaging of single cell ‘omics’ such as DNA-, RNA-, protein- and metabolite-analysis.
  - Understand, at the single cell level, processes such as cellular differentiation, specialization, and responses to external factors such as drugs. Apply computational modelling, simulations and advanced computational methods to achieve this predictive understanding and progress to more complex systems (tissues, organisms).

Milestones:

- Insight in the impact of the heterogeneity of proteins and protein complexes on cellular networks

- Influence of heterogeneity in the dynamics of bio molecular networks and on the robustness of systems.
- Impact of (epi-) genomics on the heterogeneity of individual cells, cellular dynamics, differentiation and interactions with the environment.
- Utilize the knowledge on network dynamics and cellular heterogeneity to tackle main societal challenges.

Expected result present- 2040:

Scientific/technological goal: An understanding of the dynamics of networks and cellular heterogeneity will provide a deeper understanding of the collective behaviour of cells such as in cell populations, tissue and organs. Develop predictive models for system robustness.

Industrial end goal: Application of single cell network theory describing meta-stability in the regulation and functioning of processes such as in plant breeding, antibiotics resistance (persistence), the productivity of micro-organisms in biotechnological applications, and bio-inspired materials.

Societal goal: By studying individual processes, important insights will be obtained in the mechanism of aging, cellular differentiation and disease (for instance, the onset of cancer development and neurodegenerative disease), as well as in medical treatments that affect the behaviour of individual cells ultimately contributing to the central mission of the KIA Health & Care.

3.3.2 Engineering of molecules and cells

During the last decades, technological advances enable the modification of biological materials at an advanced level. This involves DNA reprogramming and substitution, control of protein production but also the reconstitution of protein complexes, membranes and other macromolecular structures such as the cytoskeleton which links to the Advanced Materials cluster within the KIA Key technologies. Also, synthetic parts with self-assembling properties can be generated such as complex DNA structures (DNA origami) and membranes. Further advances in reconstitution and synthesis methods will enable more directed modifications and the construction of hybrid systems. This technological advance will enable and further the directed design and construction of cells. We propose to add networked capabilities to cells to increase their functionality; to construct a minimal cell that is able to perform a basic level of gene regulation, homeostasis with its environment and that even can divide; to build a functional organelle; and to create functionally interacting cellular systems such as an “Organ-on- a-Chip”. In addition, cell-like entities with coupled complex functions can find many applications in medicine and material development; in diagnostics, and to collect information on the chemical status in a body and report back via non-invasive imaging, to prepare dynamic self-assembling structures, to promote complex series of catalytic steps, to deliver therapeutic agents to specific (sub)tissue locations with variable controlled local release or modified local reactions, to stimulate and participate in tissue repair. Especially the diagnostics and the information on the chemical status in a body contributes to the KIA Health & Care, mission I (lifestyle and environment), mission II (access to Healthcare) and mission III (chronic diseases).

To achieve this:

In order to build functional cells and cellular systems both a bottom-up and top-down approach is needed. In the bottom-up approach we have to identify the chemical components and their relevant interaction networks to generate systems with increasing complexity and predicable function. In the top-down approach, existing cells and cellular systems are exploited and modified to re-programme their function for specific tasks. This also involves harnessing cell heterogeneity for complex functions including mimicking organs.

Specific steps required present-2040:

I. Development of synthetic and chemical biology, bottom up

Development of a synthetic cell from building blocks capable of performing basic reactions such as lipid biosynthesis, gene regulation, protein synthesis, ion homeostasis and division. Identify the minimal requirements to generate an autonomously operating system based on a minimal synthetic genome.

II. Development of synthetic and chemical biology, top down.

- Development of minimal cells. Identify the requirements to speed up genome editing for genome minimization and the introduction of complex multi component biosynthetic pathways and specialized cell factories.
- Development of multicellular biological model systems such as "Organ-on-a-Chip". Identify the requirements to generate a robust system for high throughput screening.
- Development of synthetic microbial communities for specific tasks in bioremediation, biobased fuels, food and health

Milestones:

- Multidisciplinary virtual centre of Synthetic biology.
- Minimal cells that conduct specific biochemical reactions in a robust manner and that can be used in industrial applications related to bioenergy, biomaterials, chemical production.
- Synthetic cell that in a controlled manner carries out basic biochemical reactions and that can replicate.
- Synthetic cells with diagnostics or drug delivery functions
- "Organ-on-a-Chip" modules that can be used as a disease specific screening platform.
- Synthetic microbial communities to support the gut microbiome

Expected result present- 2040;

Scientific/technological goal: Assembly of biochemical reactions into functional cellular concepts up to the creation of a minimal functional cell.

Industrial end goal: Designer minimal cells for application and production in bioenergy, biomaterial and (bio)chemical production which supports the missions as formulated in the KIA LWV and the KIA Circular Economy and to the cluster Advanced Materials in the KIA Key Technologies; Tailor made platforms for high throughput drug screening.

Societal goal: Alternative systems to replace animal testing in the development and clinical testing of medicines. Cell like entities as smart diagnostic and therapeutic agents, improving health and healthcare. Thus supporting the central mission of the KIA Health & Care

Examples of MJPs related to this pillar:

MJP01 Fenotype-Genotype-Prototype

MJP02 Building Blocks of Life Begrip en benutting van cellulaire sytemen

MJP06 Verbetering van de fotosynthese-efficiëntie

MJP14 Maatschappelijke gewenste en veilige biotech toepassingen door Safe-by-Design

MJP17 Biomedical Engineering for Health

MJP86 Bridge – Life Science Technologies

MJP92 Medische Isotopen

Examples of connections to other platforms:

Gravity Programs such as BaSyc (synthetic cells), Netherlands Organ on a chip initiative, Institute of Chemical Immunology, Cancer GenomiCs.nl, Roadmap Infrastructure Proteins@Work, uNMR.nl, and Nanofront, Kluyver Centre for the genomics of industrial fermentations, BE-Basic (on sustainable biobased processes), Centre of Synthetic Biology at the University of Groningen, BioSolar Cells, Top Institute Food and Nutrition (TIFN), Human disease model on a chip (hDMT), research facility UNLOCK (Unlocking microbial diversity for society) and FOM Institute AMOLF.

Contribution of this Chemistry of Life roadmap to the Mission driven research

- (Bio)chemistry supports the missions formulated in the KIA Circular Economy which also aims for optimal use of resources, including biological resources and manufacturing processes.
- Identification of new, optimal chemical processing of new, sustainable sources for protein supply which enforces the KIA Circular Economy; MMIP2AQ3
- Adapt feeds to reduce nitrogen, phosphate and/or sulphur emission which enforces the KIA Circular Economy; MMIP2AQ11.
- Utilize the knowledge on network dynamics and cellular heterogeneity to tackle challenges in energy, food and health(care).
- New, biochemical derived health promoting substances, including enzymes and micro- organisms is linked with life science technologies: ST7-4 Gene Editing / Precise Genetic Engineering Q6
- Wearable diagnostic devices eliminate the need for visiting the hospital, are instrumental to avoid clearly dangerous environmental chemical entities or enable to remove these from environment (smart filters/absorbers) and prevent disease) and directly enforces Mission II, access to healthcare (KIA Health & Care)
- Explore new functionalities of Materials in human bodies (e.g. stability, release, mechanical strength, lubrication, antimicrobial, molecular detection and reporting) which enforces the cluster Advanced Materials in the KIA Key Technologies.
- Creation of new chemical, molecular, biological and cellular entities to interact with and predictably modify chemical properties of biomolecules for treatment (e.g. eliminate cancer cells, restore neuronal function, repair degenerated joint tissue, kill microbes and virus infected cells, or prevent infection, stimulate immune responsiveness specifically to diseased cells, address orphan diseases) Explore new functionalities of Materials in human bodies (e.g. stability, release, mechanical strength, lubrication, antimicrobial, molecular detection and reporting) which enforces the cluster Advanced Materials in the KIA Key Technologies
- Design and synthesis of new (bio)molecular entities which enforces the cluster Chemical technologies in the KIA Key Technologies
- Through this Chemistry of Life roadmap, new sources of e.g. proteins are currently being implemented and food is improved chemically which requires a detailed molecular understanding of (plant) cellular mechanisms to support the mission of feeding the ever-increasing world population in a sustainable manner which is also addressed in the KIA LWV and the KIA Circular Economy. Chemistry is instrumental in the transition away from animal-based protein supplies towards more environmentally friendly plant-based protein sources with their associated reduction of greenhouse gas emissions and supports the related missions formulated in the KIA LWV and the KIA CE
- Less spoilage of foods as formulated in the missions of the KIA LWV and the KIA CE by exploring biochemical production and use of new nature inspired preservatives,
- The chemical knowledge generated for diagnostics and the information on the chemical status in a body contributes to the KIA Health & Care, mission I (lifestyle and environment) and mission III (chronic diseases).
- Designer minimal cells for application and production in bioenergy, biomaterial and (bio-)chemical production as described in pillar 3 of this roadmap support the missions as formulated in the KIA LWV and the KIA Circular Economy and to the cluster Advanced Materials in the KIA Key Technologies; Tailor made platforms for high throughput drug screening.
- Cell like entities as smart diagnostic and therapeutic agents as described in pillar 3 of this roadmap contribute to the improvement health and healthcare the overall aim of the KIA Health & Care.

Connections / Cross Overs

The Chemistry of Life program has been initiated to strengthen the collaboration within the different programs of TKI Chemistry as well as across the different TKIs. This is important as we realize that innovation doesn't happen is silos (competing for limited resources) but at the interface of different disciplines and by multi-disciplinary contributions and collaborations (sharing limited resource).

While the current roadmap has been designed from the identified specific needs and opportunities in Chemistry of Life, it is not surprising that many desired connects exist with other TKIs and EU initiatives. Some of these connections are presented in table 2 which shows that all (!) proposed tasks and actions of Chemistry of Live are strongly connected. These connections can be worked out for example in designing joint (cross TKI) calls. In these joint calls the contribution (or knowledge gap) of the different disciplines will become visible and might further guide priority setting driven by specific innovation themes.

Chemistry of Life	TKI Chemistry	TKI LSH	TKI Agri/Food	TKI Biobased	TKI HTSM	Horizon 2020	Potentially interested companies
Activity 1.1		-Molecular diagnostics -Imaging			-Diagnostics (incl. imaging)	-Health, demographic change and wellbeing	DSM, Akzo, Unilever, multiple (> 100) start- ups in biotech
Activity 1.2		-Pharmacotherapy -One Health (Antimicrobial resistance)				-Health, demographic change and wellbeing	Synthon, MSD, Janssen, Galapagos, multiple (> 100) start-ups in biotech
Activity 1.3	-Advanced Materials (Materials with added functionality)	-Regenerative medicine			-Enabling technologies (Biomaterials)	-Health, demographic change and wellbeing	DSM, Philips,
Activity 2.1			- Proteins, Carbohydrates, Oils			-Food security, sustainable agriculture	FrieslandCampina, Unilever, AVEBE, Danone, Cosun
Activity 2.2		- Specialized Nutrition Health	- Roadmap health (e.g.			-Food security, sustainable agriculture	FrieslandCampina, Unilever, AVEBE,

		and Disease	healthy aging)			-Health, demographic change and wellbeing	Danone, Nestlé
Activity 2.3	- Chemical conversion, processes and synthesis (Biomass and renewable resources)		- New adapted feedstock -Ligno-cellulose as feedstock	- Bio-refinery: Proteins, oils, carbohydrates separation, nutritional and pharma products from plants		-Food security, sustainable agriculture -Climate action, environment, resource efficiency and raw materials	FrieslandCampina, Unilever, AVEBE, Danone, Nestlé
Activity 3	- Nanotechno-logy (e.g. energy storage) - Chemistry & Physics; Fundamentals for our future, Rapport Commissie Dijkgraaf	- Regenerative Medicine - Enabling Technologies	- Roadmap health (e.g. metabolic programming)	- Solar capturing (incl. micro-organisms)		-Health, demographic change and wellbeing -Food security, sustainable agriculture -Secure, clean and efficient energy	

Table 2

Task 1: Molecular entities, devices and approaches for understanding, monitoring and improving precision healthcare

1.1 Development of analytical, biophysical devices and cellular model systems

1.2 Creation of new chemical, molecular and cellular entities

1.3 Biomedical Materials for improved functionalities

Task 2: Molecular entities, technologies, devices and approaches for understanding, monitoring and improving food to ensure a sustainable supply of safe and nutritious, delicious food and feed to optimize health and wellbeing

2.1. Biochemical tailoring of food

2.2. Understanding food digestion and metabolism to increase nutritional availability and health

2.3. Sustainable production and consumption

Task 3: Enabling technologies and approaches for fundamental understanding, monitoring and improving molecular entities in the Chemistry of Life

3.1 Understanding of cellular processes from molecule to organism

3.2 Engineering of molecules and cells