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## **New pathogens in beef and cow's milk products: More research required**

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In February 2019, the German Cancer Research Centre (DKFZ) presented findings on new infection pathogens that go by the name of “Bovine Milk and Meat Factors” (BMMF). According to these findings, the previously unknown pathogen can cause inflammations. According to the DKFZ, they have been detected up to now in cow's milk, cow's milk products and the blood serum of healthy cattle. From the scientific findings made up to now, it seems possible that an indirect connection could be interpreted between the consumption of various foods originating from cattle and the occurrence of several cancer types in humans. The DKFZ is assuming that infants whose immune system has not yet fully matured become infected with BMMF during their first year of life through supplementary feeding with cow's milk. They therefore conclude that infants should not be given cow's milk too early.

According to the DKFZ, BMMF are a new pathogen similar in type to both viruses and bacteria. Because they are related to plasmids, they are currently being called “plasmidomes”. As far as can be established by the DKFZ researchers, the BMMF do not occur as “naked” genetic material but rather together with proteins.

The German Federal Institute for Risk Assessment (BfR) and Max Rubner-Institut (MRI) jointly conclude that an assessment of the possible risks posed by so-called BMMF as possible cancer risk factors has not been possible up to now due to the inadequate data situation. The presumed connection between the BMMF and the incidence of cancer in humans should be examined further.

In line with the latest available information regarding nutrition, the BfR and MRI agree with the following recommendation: On the basis of the epidemiological studies published up to now on the connection between the consumption of red and processed meat and an increased risk of colon cancer and in concurrence with the German Nutrition Society (DGE), it is recommended that meat consumption be limited to a maximum of 600 grams per week. Contrary to this, the consumption of cow's milk without any restriction is still recommended in compliance with the latest available knowledge. Breastfeeding in order to prevent various diseases is also fundamentally advocated.

The German Federal Institute for Risk Assessment (BfR) and Max Rubner-Institut (MRI) have assessed a press release on an event held at the German Cancer Research Centre (DKFZ) in Heidelberg on “new infection pathogens from milk and meat as cancer risk factors” and state their joint position on this in the following paragraphs.

### **Background of the DKFZ press release**

In the opinion of the DKFZ, a certain class of pathogens in beef and milk, the so-called “Bovine Meat and Milk Factors” (BMMF), could be the cause of chronic inflammations which could form the basis for a malignant degeneration of cells in the breast and colon. According to the DKFZ (2019) and zur Hausen et al. (2017), the geographical distribution pattern of the incidence rates of colon and breast cancer indicates a close connection with the consumption of milk and meat products from European cattle (*Bos taurus*).

According to the documents provided at the DKFZ press conference (2019), BMMF are single-stranded, ring-shaped DNA elements which bear a great similarity to the sequences of specific bacterial plasmids. All BMMF known to date each possess a gene for the “rep” protein (replication initiator protein) required for their own replication, irrespective of other genes which may exist. According to Eilebrecht et al. (2018), most BMMF show a similarity to plasmids of the species *Acinetobacter baumannii*, although several BMMF also have similarities with certain viruses with small, circular, single-strand genomes (DKFZ, 2019). Furthermore, they probably do not occur in nature as naked DNA but rather in association with proteins. BMMF constitute, according to DKFZ, a new class of pathogens whose characteristics lie between viruses and bacteria. Due to their relationship with plasmids, they are therefore currently being referred to as “plasmidomes”. The DKFZ points out that it has not been possible to clearly define the nature of these pathogens up to now.

Over 120 different types of BMMF DNA have been isolated until now from commercially available cow’s milk, cow’s milk produce and from serum samples from healthy cattle (Whitley et al., 2014; Falida et al., 2017; DKFZ, 2019). A replication of various BMMF in human cells was proven (Eilebrecht et al., 2018), whereby the pathogens depend on cellular proteins which have not yet been determined. Furthermore, serum antibodies against BMMF were detected in a total of 350 individuals (healthy people and cancer patients), thus proving exposure to the pathogen. According to the DKFZ, BMMF proteins have been found up to now in the colon, prostate gland and brain, whereas BMMF DNA was detected in the human colon. However, no BMMF sequences have been detected yet in tumour cells.

Areas of tissue infected with BMMF show increased levels of reactive oxygen compounds, which are a typical characteristic of inflammations and which favour the development of genetic changes. Due to the observations mentioned, especially the epidemiological ones, the DKFZ is assuming that an infection with BMMF can result from the consumption of dairy products and/or beef, especially among infants whose immune system has not yet fully developed. No indications of a possible time of infection are to be found in the literature. The immune system is not fully developed at birth, or it works at a reduced level, according to the latest findings (Ulas et al., 2017), and develops itself further step by step through exposure to antigens during childhood (Simon et al., 2015). However, infection at a later stage of life with a fully developed immune system cannot be excluded at present.

After infection, the pathogens are said to induce a chronic-inflammatory reaction in certain tissues (colon, breast) which can promote the development of cancer in the surrounding tissue (especially colon cancer, possibly also breast and prostate cancer). The outbreak of the disease is not expected to occur until decades after the actual infection (zur Hausen et al., 2019). BMMF are thought to have an indirect carcinogenic effect here, meaning that they are not involved directly in the cancer-promoting molecular processes of the cells but create a – usually inflammatory – carcinogenic environment. For the stated reason, the DKFZ concludes that there is no direct causality between an infection with BMMF and colon cancer, for example, but that the BMMF share a portion of the risk of colon cancer which cannot be exactly quantified (DKFZ, 2019).

The DKFZ mentions breastfeeding over a longer period (over 6 months) as a possible preventive measure against infection with BMMF. Breast milk contains numerous ingredients with antipathogenic properties (Peterson et al., 2013). These often contain glycan structures, i.e. sugars, which occur either as free oligosaccharides (human milk oligosaccharides) or bound as macromolecules in the form of glycoconjugates (glycoproteins and glycolipids) (Peterson et al., 2013; Morozov et al., 2018). Human milk glycans are capable of mimicking the recognition points for pathogens, binding themselves to them and hindering the pathogens

from adhering to cell surfaces, thus preventing infections (Newburg et al., 2009; Peterson et al., 2013; Morozov et al., 2018). Breastfeeding goes hand in hand with a reduced risk of infection with various pathogens (e.g. rotaviruses), especially if infants are exclusively breastfed over the first 6 months (Krawczyk et al., 2016; Quigley et al., 2016). It cannot therefore be ruled out, and it is generally conceivable as a hypothesis, that human milk glycans could also protect against infections with BMMF. This hypothesis cannot be substantiated at the moment, however, due to a lack of data.

The evidence of a connection between early feeding with breast milk and the risk of cancer of the progeny in adulthood is limited. The best research has been conducted on the association with breast cancer, but the results are inconsistent (Ekbohm et al., 1993; Freudenheim et al., 1994; Weiss et al., 1997; Titus-Ernsthoff et al., 1998; Martin et al., 2005; Wise et al., 2009).

## Assessment

As explained above, it is currently not possible to determine or define the exact nature of BMMF. The above-mentioned observations – especially the epidemiological ones – can be interpreted as preliminary indications of a possibly indirect connection between the consumption of various foods of bovine origin and the incidence of certain types of cancer in humans, but they do not show a causal connection.

Valid, evidence-based examinations have been missing up to now to estimate the potential risk. There is a lack of data, for example, on the occurrence of BMMF in other foods of non-bovine origin, on the occurrence of BMMF in healthy people compared to cancer patients, on the mechanism of inflammation and cancer induction through BMMF, and on the infectivity and inactivation of BMMF in foods. The estimation of a connection between the consumption of bovine foods containing BMMF and the incidence of tumour diseases seems barely possible at the moment, since the BMMF are only supposed to act as indirect carcinogens and after a very long latency period.

Moreover, the epidemiological studies published up to now must be seen in a differentiated way. In the case of intestinal tumours, the studies published to date indicate that the consumption of red and processed meat correlates with the occurrence of colon cancer (WCRF, 2007; Huxley et al., 2009; Chan et al., 2011; Corpet, 2011), but that a high consumption of milk and dairy produce is accompanied by a reduced risk of colon cancer (WCRF, 2007). According to the WCRF (2018), neither the consumption of red meat nor of cow's milk results in increased incidence of breast cancer.

## Conclusion

An assessment of the hazards posed by so-called “Bovine Meat and Milk Factors” (BMMF) as possible cancer risk factors is currently not possible due to a lack of data.

On the basis of the epidemiological studies published to date with regard to the connection between the consumption of red and processed meat and increased risk of colon cancer, and in concurrence with the German Nutrition Society (DGE) it is recommended to limit meat consumption to a maximum of 600 g/week. Contrary to this, the consumption of cow's milk without any restriction is still recommended in compliance with the latest available knowledge.

Breastfeeding as a preventive measure against the occurrence of various diseases is fundamentally to be advocated. With regard to the prevention of an infection with BMMF, however, valid data is currently also lacking here.

#### More information on the topic of viruses in food at the BfR website

Viruses

[https://www.bfr.bund.de/en/a-z\\_index/viruses-130212.html](https://www.bfr.bund.de/en/a-z_index/viruses-130212.html)

Scientific publication on polyomaviruses in beef

[https://www.bfr.bund.de/en/detection\\_and\\_genome\\_characterization\\_of\\_bovine\\_polyomaviruses\\_in\\_beef\\_muscle\\_and\\_ground\\_beef\\_samples\\_from\\_germany-240042.html](https://www.bfr.bund.de/en/detection_and_genome_characterization_of_bovine_polyomaviruses_in_beef_muscle_and_ground_beef_samples_from_germany-240042.html)



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## About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. It advises the Federal Government and Federal Laender on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.

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