

## COMMENTARY

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# Is Phosphorus the “Key” of cancer?

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### Summary

Bobko et al. reported a very interesting article concerning the impact of interstitial inorganic phosphate (Pi) on tumor progression. Previous studies have shown that blood levels of Pi might be related with either the presence or growth of cancer in the human body. Heroin-addicted persons have normal values of Pi, while the incidence of cancer in these

individuals seems to be very low. The question rises: Is Pi the key of cancer? Further studies are definitely needed, focusing on the correlation between inorganic Pi and cancer.

**Key words:** cancer, phosphorus

### Comment

We read with great interest the important article by Bobko et al. entitled: “Interstitial Inorganic Phosphate as a Tumor Microenvironment Marker for Tumor Progression” [1]. The authors have employed a new multifunctional trityl paramagnetic probe and electron paramagnetic resonance technique for *in vivo* measurements of interstitial inorganic phosphate (Pi) in various mouse models of cancer. The authors reported dramatic differences, about 2-fold higher concentrations for interstitial Pi in tumors in contrast with normal tissues. Eventually they reported that the only parameter that also allowed for discrimination between non-metastatic and highly metastatic tumors was the higher concentration of Pi. Higher Pi values were associated with changes in tumor metabolism and supported different mechanisms of protons and Pi accumulation in tumor microenvironment (TME), supporting the evidence that interstitial Pi is a new TME marker for tumor progression.

It has been previously reported that the growth of cancer in the body is associated with increased phosphorus in the blood [2]. On the other hand, increased phosphorus in the blood when some other causes are excluded, might indicate that somewhere in the body cancer is growing [3]. In addition, it has been shown by Kuang et al. and de Carvalho et al. that if the amount of phosphorus in the blood of a cancer patient can be reduced to half, then the size of the tumor will be reduced to three quarters [2,4]. Uptake of phosphorus inside the cell environment seems to play an important role in cancer growth [5].

In a recent report it has been demonstrated that the amount of phosphorus in heroin abusers – who had never stopped taking the drug – was in normal levels and they never developed cancer [6]. This has been also confirmed with a statistical review in the period between 2001 and 2010 of the Greek Reitox Focal Point regarding 2321 deaths of

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heroin addicts and no-one had died of cancer [7]. This means that probably heroin does not allow phosphorus to increase above the normal levels.

Research, now being in progress at the National Cancer Institute “Agiros Savvas”, Athens, Greece, reveals that previous heroin addicts being under methadone detox treatment develop cancer as all the other people, and this has an explanation: It is known, since 1949 that “methadone (in very dilute solution) does not change the rate of uptake of phosphate ions by the red blood cell” [8]. This means that methadone does not restrain the phosphorus with an end result of cancer growth.

Phosphorus is known to have an important role in the metabolism of cells, especially during mitosis. Marshak in 1940 was the first to report that after administration of radioactive phosphorus to mice with cancer of the liver, cancer cells contained more radioactive phosphorus than the normal liver cells [9]. His report has been followed by others who confirmed Marshak’s findings in humans. These findings were reconfirmed by innumerable other investigators reporting that in cancer the amount of phosphorus in the organism/blood is generally increased and cancer cells/tissues take up approximately six to seven times more than normal ones [10-12].

Consequently, based on previous studies as well as on the study from Bobko et al., we may also conclude that:

1. The amount of phosphorus in the blood increases in all cancer patients [2]. However, it differs in treated and untreated tumors [13].
2. The amount of phosphorus in the blood varies according to the stage of disease at presentation in cancer patients with lung cancer [14].
3. The amount of phosphorus in the blood of regular heroin addicts and normal subjects is in the normal levels [6]. Regular heroin users probably do not develop cancer because heroin acts as a “barrier”, not allowing the increase of phosphorus above the normal values [7].
4. If phosphorus could be excluded from the process of development and growth of cancer, it might not ever evolve [2].
5. Higher Pi content seems responsible for tumor growth and progression [1].

The role of phosphorus is more than essential - “might be the key”- in the development and growth of cancer [15]. It is our opinion that Bobko et al. have made a breakthrough in the deep understanding of Pi in the development of cancer. As Bobko et al. [1] have written: “Pi association with tumor metabolism, buffer-mediated proton transport, and a requirement of high phosphorus content for the rapid growth in the growth rate hypothesis may underline its potential role in tumorigenesis and tumor progression”. This should not be underestimated. Further studies are definitely needed. The Future will show.

## Acknowledgement

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