THE IMPORTANCE OF MITOGENETIC RAYS IN THE SYNTHESIS OF PEPTIDES IN THE LIVER

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In 1937-1938 A.G. and L.D. Gurvich [1, 9] showed that during irradiation of mixed solutions of amino acids with mitogenetic rays, compounds of relatively high molecular weight were formed, which, on digestion with gastric juice, produced mitogenic rays of a spectral composition identical with that characteristic of the peptide bond.

This work was of great importance in principle since it showed the possibility of in vitro synthesis of biologically important compounds by a photochemical rather than an enzymic method. These workers put forward the hypothesis that in the living organism, thanks to the mitogenetic system, peptide synthesis may take place by a photochemical method in addition to and without the participation of enzymes.

A.G. and L.D. Gurvich [3] further showed the identity of the energy requirements for stimulation of peptide synthesis and cellular division by mitogenetic rays: both peptide synthesis and cell division can be brought about by any wavelength of the mitogenetic spectrum from 1900 to 2700 A for irradiation in darkness and to 3260 A for irradiation in light or in infrared radiation. This convinced these workers of the great biological importance of the fact that the mitogenetic action of ultraviolet light begins with stimulation of peptide synthesis.

It must be pointed out that suppression of mitogenetic rays by the administration of a tumor-destroying agent or of extinguishers of mitogenetic rays in living objects leads to a sharp fall in the number of dividing cells [3, 4] and at the same time to marked vacuolization of the protoplasm of the majority of even the young cells while in many cases the whole body of the cell appears as one continuous vacuole. This condition, analogous to that observed in the rootlets of bean plants whose cotyledons have been cut off, is usually attributed to protein starvation of the cells.

In 1945 A.G. and L.D. Gurvich [10] introduced a new method of mitogenetic spectral analysis with selective dispersion, making it possible to compile an atlas of the characteristic spectra of functional molecular groups or, in some cases, of whole molecules of various organic compounds.

Because of its sensitivity, this method permits the analysis of extremely transient processes taking place in vitro and in vivo as rare events. By means of this method E.A. Ternovskaia (cited in [11]) obtained more direct experimental proof of peptide synthesis by mitogenetic irradiation of amino acid mixtures.

In 1953-1954 A.G. and A.A. Gurvich (cited in [11]) showed that in the dark, peptide synthesis in the leaves of green plants takes place less intensively than in the light, since only in the light do mitogenetic rays arise in them (according to N.M. Peredel'skaia [7]) in consequence of summation of the energy of the photons of visible light to the level of ultraviolet radiation. In plants kept in the dark, peptide synthesis may be stimulated by irradiation with mitogenetic rays, but in plants grown in the light it is inhibited by suppression of mitogenetic rays

by means of injection of the so-called extinguishers.

During prolonged action of extinguishers the diminution in protein synthesis is so considerable that growth of the experimental plants is retarded in comparison with controls. These results obtained by A.G. and A.A. Gurvich (cited in [11]) confirm the necessity of mitogenetic rays for peptide synthesis in the green leaves of plants.

In 1934 A.G. and L.D. Gurvich [2] found that in contrast to all other organs the liver and kidneys of animals on a normal diet do not produce mitogenetic rays. A.G. Gurvich expressed the view that as a result of the fact that processes of syntheses were predominant in the liver, it contains only an insignificant amount of the so-called fluorescents – low molecular compounds able to emit energy in the form of rays. High molecular compounds – proteins, glycogen and so on – do not fluoresce. Hence it followed in the first place that the liver of fasting animals in which processes of breakdown are predominant may possibly emit ultraviolet light, and in the second place that injection of fluorescents into normally fed animals should lead to emission of rays from their livers. Both these conclusions derived from A.G. Gurvich's hypothesis have been confirmed experimentally in work by E.A. Ternovskaia and V.F. Eremeev (cited in [11]).

The results of the investigations by E.A. Ternovskaia and V.F. Eremeev, and also reports in the literature on the synthesis of proteins in the liver of normally fed animals and of protein breakdown in the liver of fasting animals have enabled the study of the importance of mitogenetic rays in peptide synthesis in the liver to be undertaken.

It must be pointed out that the majority of authors [5, 6, 12, 13, 14, 15, 16] consider that the liver plays a great part in synthesis during protein metabolism, and assume that the liver has the power to accumulate proteins which are mobilized to meet the needs of the body during protein starvation more rapidly than proteins of other organs (especially in the first stages of starvation).

In this connection it might be supposed that in early stages of an animal's starvation the breakdown processes of protein substrate are still so ill-developed that the quantity of fluorescents formed in this way is not sufficient to reveal even threshold intensities of mitogenetic radiation. At the same time there is quite enough of them to reveal breakdown processes of protein substrate by the method of spectral analysis with selective dispersion.

If this hypothesis of A.G. Gurvich could be confirmed experimentally, an attempt might be made to irradiate the liver externally from some mitogenetic source and cause partial resynthesis of the protein substrate, which could be judged by the threshold exposures necessary to show selective dispersion of NH_2- and OH-groups, the amounts of which are increased during breakdown of protein substrate and decreased during its resynthesis. This investigation forms the content of the present paper.

EXPERIMENTAL METHOD

White mice were kept for 18 to 20 hours on a fixed diet (millet, white bread and milk). An excess of food was given to the animals. At the conclusion of this period they were totally fasted. Fasting lasted from 3 hours 30 minutes to 5 hours 30 minutes.

It was first established that radiation appeared in the liver during starvation of the animal for 5 to $5\frac{1}{2}$ hours.

Further experiments were performed in accordance with the following scheme. After fasting for four hours it was checked whether there was spontaneous radiation in the liver of the animal, and the selective dispersion spectrum of the amino groups was taken. Next the liver was irradiated for 15-30 minutes with mitogenetic rays from a source of radiation and the selective dispersion spectrum of the amino groups of the protein substrate again taken at different exposures. In this way, in the first series of experiments the selective dispersion spectrum was taken from the same aspect (ventral) as the lobe of the liver irradiated; in the second series of experiments, from the opposite aspect, i.e., the liver was irradiated on the dorsal aspect and the spectrum taken from the ventral aspect.

In order to obtain full confirmation that all the manipulations carried out on the liver were not affecting its condition, special control experiments were set up in which everything was done to the liver just as has been described, but it was not irradiated from a source of mitogenetic rays.

EXPERIMENTAL RESULTS

The results of all the experiments are shown in the table.

It follows from the table that spontaneous emission of rays does not occur with fasting for four to five hours, and the amino groups of the protein substrate of the liver can be revealed by their selective dispersion at exposures of 10-12 seconds and that after mitogenetic irradiation of the liver these amino groups cannot be detected, not only at exposures of 10-20 seconds, but also of 15, 20 and 25 seconds, and they are demonstrable only at exposures exceeding 30 seconds; furthermore the same results are found when the liver is irradiated on its dorsal aspect and the spectrum taken from its ventral aspect. The manipulations carried out on the liver do not affect its condition in any way, as shown by experiments in which no irradiation was carried out and the amino groups of its protein substrate were revealed at exposures of ten seconds, as also occurred without manipulations after the same period of fasting.

Mitogenetic Spectra of Terminal NH_2-Groups of Peptides in the Liver of Fasting Mice Before and After Irradiation

Period of fasting	Exposure (in seconds)	Spectral band 2060-2070 A. Mean effect (in %)	Spectral band 2260-2270 A. Mean effect (in %)	Number of experiments
Spontaneous radiation from the liver of fasting mice				
3 hours 30 minutes to 5 hours	10-15	1.0	1.3	18
5 hours 30 minutes	10	40.3	58.0	3
Selective dispersion of the liver of fasting mice				
4 hours 10 minutes to 5 hours 25 minutes	10-12	34.3	33.9	18
Selective dispersion of the liver of fasting mice after irradiation from a source of mitogenetic rays for 15-30 minutes				
4 hours 20 minutes to 5 hours 40 minutes	12	0	2	5
	15	−1	0	4
	20	−1	1	4
	25	0	2	3
	30	37	32	3
Selective dispersion of the liver of fasting mice after performing all steps of the experiment except mitogenetic irradiation				
4 hours 50 minutes to 5 hours	10	27.3	44.0	3

The results obtained show that in the liver of mice at early stages of fasting (four to five hours) processes have already begun which can be detected by the method of spectral analysis of selective dispersion. Increase in the intensity of these processes leads to the appearance of spontaneous emission of rays by the liver after fasting for five hours.

Irradiation of the liver of fasting mice from a mitogenetic source increases the threshold exposures necessary for detecting the terminal amino groups, which proves that they have diminished in quantity and is accounted for by the partial resynthesis of the protein substrate of the liver tissue.

The discovery of a reduction in the quantity of terminal amino groups during irradiation of the liver on its dorsal aspect and taking the spectrum from its ventral aspect shows that the processes of partial resynthesis of the protein substrate as a result of mitogenetic irradiation have a chain character and involve the whole thickness of the liver.

It thus follows from the results of the work described that mitogenetic rays stimulate peptide synthesis in the liver of animals.

How does peptide synthesis take place in the normal liver which does not emit rays but which acquires the power of radiation when fluorescents are administered to it? In order to answer this question it is necessary to remember how mitogenetic rays arise during enzymic reactions: the large quanta of energy given out during recombination of free radicals or atoms, arising as rare phenomena in enzymic processes, are absorbed by neighboring molecules which then emit the absorbed energy in the form of mitogenetic rays.

Since fluorescents (molecules emitting energy in the form of rays) are present in the liver in small concentrations, photons of mitogenetic rays arise so rarely that radiation cannot be found even by biological detectors, but nevertheless peptide synthesis may take place at subthreshold intensity.

Another factor stimulating synthesis of peptides may probably be the above-mentioned quanta of energy, which are emitted quite irrespective of whether there is an adequate concentration of fluorescents.

These considerations just mentioned lead us to the hypothesis that the liver of animals which are affected by malignant neoplasms, containing a cancerous suppressor of mitogenetic radiation preventing the formation of large quanta of energy, is, despite the influx of all necessary food substances, in a state of protein starvation to some degree, in consequence of the absence of the necessary energy conditions for peptide synthesis.

The experimental verification of this hypothesis will be dealt with in a special paper.

SUMMARY

The first traces of disintegration of the protein substrate of the liver (in situ) were revealed in hungry animals by the method of mitogenetic spectral analysis of selective scattering of the ultraviolet radiation when the animals were fasted for four to five hours. Resynthesis of the protein substrate of the liver may be caused by irradiation of the liver with the nitrogenetic source of radiation during these "hungry" periods. Thus, stimulation of the peptide synthesis by the mitogenetic radiation may be demonstrated.

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