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Unexpected results in a number of experiments in high-energy and medium-energy nuclear physics are chipping away one of the cornerstones of nuclear physics, namely the pi meson (or pion) as a dominant carrier of the nuclear force. In the 1930s, H. Yukawa suggested that nuclear forces would have particles associated with them, and the discovery of the pions in 1947 was a beautiful confirmation of his prediction. Since then, many more mesons have been found and our understanding of the nuclear force has been refined and modified to include contributions from all the meson exchanges that could occur. Nevertheless, the pion has special importance because it is the lightest of the mesons. According to the Yukawa theory, the smaller the mass of the particle, the larger the distance over which the force acts. The pion force should therefore dominate at distances as large as the average spacing between nucleons in a nucleus. This large distance behavior has been well established experimentally; for example, the forward-angle scattering between nucleons verifies the presence of the pion field and even specifies its magnitude. However, at short distances the pion field is greatly suppressed, which only became evident with recent experiments.

In the Yukawa theory the field is predicted to grow stronger the closer one comes to the center of the nucleon, and this leads to both physical and mathematical contradictions. These are avoided by mathematically smoothing out the field near the center (by the application of what are called "form factors"), but the quantitative limit of validity at short distances has never really been settled. The naïve idea that the field should behave as a Yukawa function to guite small distances, say to 0.2 fermi (1 fermi = 10^{-15} m) from the center of the nucleon, led to blatantly false physical consequences. At those small distances the pion field would be strong enough to produce a phase transition. This transition, called "pion condensation" (1), would cause nuclear matter to behave quite differently from what is seen with actual nuclei. For example, large nuclei would have crystalline rather than liquid behavior. The additional mesons present in more refined theory moderate the pion field, but it could still be



Fig. 1. The relative number of quarks in a heavy nucleus compared to those in an equal mass of deuterium. The upper curve shows the trend of the old muon scattering data, which found an enhancement of 15 to 20%. In the newer data, the enhancement has almost completely disappeared.



Fig. 2. An electron (or muon) scattering experiment to measure nuclear pions. In the upper picture, a scattering event occurs when the electron hits a quark, in the nucleon (each nucleon having 3 quarks). The pion field around a nucleon has quarks of its own which can also scatter electrons, as shown in the lower picture.

strong at intermediate distances. In these multimeson models, the pion field does not condense, but it can be greatly enhanced by the collective influence of the many nucleons in a nucleus. The field would show up in the excitations of the nucleus, particularly those induced by external pion fields.

In 1983 high-energy physics seemed to provide some confirmation of a strong pion picture. This was the experiment by a group working at CERN, the European Muon Collaboration (EMC), that measured muon scattering from nuclear targets (2). At high

SCIENCE • VOL. 259 • 5 FEBRUARY 1993

energies, the muons scatter from the quarks in the target. More quarks were found than could be accounted for by the number of nucleons in the nucleus. The interpretation (3) was that the extra quarks came from the pion field. As expected from the nuclear physics, the pion field would be enhanced by the interactions of the nucleons, giving in effect more virtual pions in a nucleus than for the same number of isolated nucleons. This experiment also showed the quarks to be depleted at higher momentum. According to the explanation by pions, this effect would be a consequence of the observed enhancement at lower momentum.

The nuclear pions should also affect the scattering of nucleons from a nuclear target (4). The most sensitive method for probing the pion field with nuclear scattering is to use polarized beams and to measure the polarization transfer. The pions' interaction depends on the nucleon spin orientation with respect to the momentum transfer direction, giving a characteristic signature to the spin transfer cross section. An experiment (5) measuring the spin behavior of scattered protons in 1986 produced the surprising result that the scattering was independent of whether the spin was along or perpendicular to the direction of the nucleon's recoil. The expected effects of the virtual nuclear pions were simply not there.

The next developments were in the highenergy domain. In later data on electron and muon scattering, the low-momentum quark enhancement in the nuclear EMC effect all but disappeared (6). This led to a completely different experiment that could show effects from the pions, an experiment measuring specifically the antiquarks in a nuclear target. The previous experiments were only sensitive to the combined charges of quarks and antiquarks. If there were a pionic enhancement, it should also show up in the antiquark distribution, since a pion contains equal numbers of quarks and antiquarks. The actual experiment measured the muon pairs produced in high-energy proton-nucleus collisions, with conditions set so the pairs would be produced by the annihilation of quarks from the proton with antiquarks from the nucleus. This is the so-called Drell-Yan process. The experimenters found no enhancement (7), making a rather persuasive case that virtual pions with momenta greater than about 400 MeV/c (where c is the speed of light) are not very important in the nucleus. In fact, other experiments using a proton target instead of a nucleus also showed a very small probability for antiquarks (8).

A last clinching piece of evidence was a new experiment measuring 500-MeV polarized-proton scattering from nuclei, published this past summer (9). In this experiment, a proton is scattered from a nuclear target and is turned into a neutron in the process. The

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charge exchange is easily brought about by absorbing or emitting a charged pion, so this reaction should be especially sensitive to the pion field. Again, the measurement of the spin dependence at medium momentum transfers found no change with respect to nucleonnucleon scattering. This experiment was sensitive to the same range of pion momenta (greater than 400 MeV/c) as was probed with the antiquark distribution in nuclei.

The conclusion is that the pion field is greatly suppressed at shorter distances. As alluded to earlier, there are compelling mathematical reasons why the pion field cannot grow too large. A strong pion field at short distances leads to singularities when renormalized in field theory, contradicting the fundamental tenets of causality and analyticity (10). This problem is avoided in the most fundamental theory of strong interactions, quantum chromodynamics (11) or QCD, by introducing gluon forces as more fundamental than mesonic forces. However, the severe mathematical difficulties in making calculations in QCD leaves open the question of where the gluon field should begin to reveal itself in the internucleon forces.

Many theorists thought that the core of the

nucleon was rather small, of the order of a few tenths of a fermi. But in fact the pion does not seem to show itself inside of about 1/2 fermi. From another modern point of view, this is perhaps not so surprising. Today the pion is not viewed as a fundamental particle, but as an excitation of the vacuum. The low mass is seen as a consequence of a basic symmetry of QCD, called chiral symmetry. This symmetry is respected only for very low energy phenomena, so from that point of view it is not likely to be useful inside the core of the nucleon. At short distances, the QCD degrees of freedom should become important and it is natural to ask about the role of the gluon fields.

The corrected electron scattering experiment from nuclei had shown the quarks to be depleted at higher momentum, but not enhanced at lower momentum, leaving a net depletion. There is a momentum sum rule for the quarks and gluons together, so the quark depletion requires a gluon enhancement. The gluon fields of nucleons certainly overlap at distances characteristic for the intermediate range nuclear forces. There is no reason why these should not be modified in nuclear matter or dense hadronic matter. An interesting area for future research would be

Genetic Models for Studying Cancer Susceptibility

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t is becoming well recognized that the development of cancer is not simply a result of random events and environmental hazards but can depend on an individual's genetic composition as well. Approximately 10% of individuals who develop melanomas, for example, carry an inborn susceptibility for that cancer. Identification of the specific genes involved has obvious implications both for detection of susceptible individuals and for the development of new treatments. Recent well-organized efforts by many groups have begun to identify several candidate melanoma susceptibility loci on the short arms of chromosomes 1 and 9. Unfortunately, as one might predict, melanoma formation involves a complex web of interacting factors whose overall design remains obscure.

Two fish of the genus *Xiphophorus*, the platyfish (*X. maculatus*) and the swordtail (*X. helleri*)—both indigenous to the jungle streams of Central America—provide an ex-

tensive genetic model for identifying melanoma susceptibility genes. These fish have a grey-silver color that is due to a uniform patchwork of small black pigment cells (micromelanophores). These cells originate as melanoblasts and differentiate through a melanocyte stage as do their human counterparts. Some platyfish have much larger clusters of pigment cells (macromelanophores) that result in visible spots. It has been known since the 1920s that when spotted platyfish mate with nonspotted swordtails, some of their progeny will develop benign melanomas and some will develop malignant melanomas.

Forty years ago Breider hypothesized that melanoma formation in *Xiphophorus* resulted from the loss of "inhibitory" genes that suppressed species-specific macromelanophore genes (1). This proposal represents one of the first references to the concept of interacting tumor suppressor genes and oncogenes. In an elaboration of the idea, Anders (2) showed that the dominant tumor formation gene (Tu) present in the platyfish is under the control of a repressor gene (R). The malig-

SCIENCE • VOL. 259 • 5 FEBRUARY 1993

to study the gluon distributions more closely.

Another idea that has been advanced is that masses of the mesons might change in the environment of the nucleus, due to quark and gluon effects (12). This could alter the balance of forces, reducing the influence of the pion field. The mass shifts might give measurable effects in the production of electron pairs in nuclear collisions, and this will be a subject of future study at heavy ion accelerators.

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nant melanomas only form in the hybrid crosses of the F_1 with the X. *helleri* if the R gene is absent (see figure).

Three years ago Schartl and his co-workers cloned the gene at the Tu locus by a reverse genetics approach-that is, by determining chromosome location, finding nearby genetic markers, and isolating the correct candidate gene (3). The gene encodes a membrane receptor tyrosine kinase, called "Xmrk" (for Xiphophorus melanoma receptor kinase), that is similar but not identical to the Xiphophorus epidermal growth factor receptor. All Xiphophorus express a 5.8-kb Xmrk proto-oncogene transcript. A separate 4.7kb transcript is only expressed in the melanomas of the fish with the Tu gene. This 4.7-kb transcript is expressed at low levels in benign melanomas and at high levels in malignant melanomas. An essential missing piece in the puzzle has been an understanding of how *R* controls the *Xmrk* gene.

Important clues to the origin of the interaction between the R and Xmrk genes have come from comparative sequence analysis of the oncogenic and proto-oncogenic forms of Xmrk, reported by Adam and his co-workers in this issue of *Science* (4). The transcripts from the two genes differ in length by 1 kb but show colinearity downstream of codon 10. The GC-rich sequences present in the 5' end of the Xmrk oncogene are missing from the oncogene and are replaced by TATAand CAAT-like sequences from another gene. Using reporter gene constructs, Adams

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