hair follicles of the newborn kitten there are 60 percent fewer MC's and nerve endings than in the adult, while the number of myelinated axons entering the follicle is about equal in young and adult animals. Therefore, during maturation new MC's must be formed together with new branches of the afferent nerve fiber. Presumably, MC's play a role in this postnatal arborization of the type 1 nerve fiber, perhaps by serving as targets for new nerve endings (*22*) and then maintaining the resulting branching pattern. For such function a substance stored in the dense-core granules might be released from MC's, but such a release would not be part of the mechanoreceptive transduction process. A role of MC's as passive abutments for the nerve endings concurs best with the electrophysiological and morphological observations.

In more general terms, our results show that the type 1 and type 2 receptors in the sinus hair follicle respond not only to a wide range of amplitudes for dynamic and static hair displacements (*17*) but also to a wide range of frequencies (from nearly 0 to about 1500 Hz). Thus, in addition to their function as displacement detectors, they respond to a range of vibratory stimuli hitherto thought to be detected only by Pacini-type cutaneous mechanoreceptors (*23*).

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Rheumatoid Factor–Like Immunoglobulin M Protects Previously Uninfected Rat Pups and Dams from *Trypanosoma lewisi*

Abstract. *The serum of lactating rats that have never been infected with the protozoan parasite* Trypanosoma lewisi *contains a rheumatoid factor–like immunoglobulin M (IgM). This IgM amplifies a specific immunoglobulin G (IgG) response to the parasite and accounts for the unusual resistance of previously uninfected lactating rats and their suckling pups to infection with* T. lewisi. *A similar rheumatoid factor–like IgM, which is induced late in the usual course of infection with* T. lewisi *in nonlactating rats, amplifies an earlier IgG response and terminates the infection. To our knowledge, this is the first description of a rheumatoid factor, which is classified as an autoimmune antibody, acting in a protective manner.*

We showed previously (*1*) that lactating rats have an unusual resistance to *Trypanosoma lewisi*, a flagellate protozoan parasite that is highly specific for rats. In particular, we found that lactating rats have a lower peak parasitemia and do not develop the second or "adult" phase of the parasitemia; thus infections in these rats last for less than half the usual time, that is, 12 days as opposed to 24 to 26 days. We also found that the serum of lactating rats that have never been infected with *T. lewisi* can agglutinate parasites of the adult phase isolated from infected, nonlactating rats. Furthermore, we observed that suckling rats infected with *T. lewisi* have a 100 percent survival rate if they are infected at 10 days of age (about the midpoint of the suckling period), but only a 76 or 55 percent survival rate if they are infected at 15 or 17 days, respectively (toward the

Table 1. Identification of the lactating rat serum factor as an IgM. Titers are expressed as reciprocals of the maximum dilution of serum or serum fraction that produced clumps of four or more parasites in every microscope field examined. Serum samples from nonlactating rats were always negative.

Treatment	Titer before treatment	Titer after treatment
Exposure to 56°C for 30 minutes	32	32
Exposure to 65°C for 30 minutes	32	0
Precipitation by 40 percent saturated $(NH_4)_2SO_4$ and redissolution of precipitate to the original volume	64	32
Three adsorptions with 5×10^8 adult parasites per adsorption per milliliter of serum	64	0
Incubation in 0.2*M* mercaptoethanol followed by dialysis against 0.02*M* iodoacetate in 0.85 percent NaCl	32	0
G-200 Sephadex chromatography	Activity recovered only in first peak, indicating a molecular weight of > 600,000	
Prior incubation of lactating rat serum (0.2 ml) with goat antiserum to rat IgM (0.1 ml)	64	0
Control incubation with normal goat serum	64	64

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end of the suckling period). Pups infected at 10 days of age showed a considerably suppressed adult phase of the parasitemia. Milk from rats agglutinated parasites of the adult phase as did pup serum under certain circumstances. From these experiments we concluded that a lactating rat serum factor (LRSF) caused agglutination of the adult parasites, enhanced protection of the lactating dams, and was transferred via milk to the pups, thereby transferring protection. We now report that the LRSF is a rheumatoid factor–like immunoglobulin M (IgM) that produces protection by amplifying a specific immunoglobulin G (IgG) response.

Using standard immunological techniques (*2*), we identified the LRSF as an IgM as shown in Table 1.

Rats infected with *T. lewisi* respond by producing an IgG antibody that inhibits reproduction of the parasite. This humoral response was first described by Taliaferro (*3*) who called it an ablastin (analogous to precipitins and agglutinins) because of its characteristic blocking effect on cell division and lack of cytocidal effects. Although it was originally thought to be a non-avid antibody, ablastin has recently been shown to be avid (*4*) and to accumulate on the parasite surface beginning on day 3 after inoculation of parasites into rats (*5*). As the parasites become coated with ablastin, metabolic changes occur and parasite morphology shifts from a so-called juvenile (reproducing) stage to an adult (nonreproducing) stage. A second IgG response occurs at about day 9 which destroys any parasites that have not become adults. The adult parasites are later eliminated by a third humoral response, an IgM that terminates the infection, leaving the rats with life-long, sterile immunity (*6*).

A major difference between juvenile parasites, which do not react with the LRSF, and adult parasites, which do so react, is the IgG coating. Since rheumatoid factors are IgM (or, less commonly, IgG or IgA) antibodies directed against autologous IgG, and since rheumatoid factor can be elicited under a variety of conditions (*7*), we considered the possibility that the LRSF might be a rheumatoid factor. In such a model, the specificity of the lactating rat serum for adult forms of *T. lewisi* would be a function of the parasite-specific ablastin IgG coating.

Trypanosoma lewisi cells free of any specific IgG were isolated from rats that had been immunosuppressed by exposure to 900 rads of whole-body radiation from a ^{137}Cs source 24 hours before they were inoculated with parasites. To prepare a source of ablastin, we collected serum from intact rats 14 days after they had been inoculated with parasites. Such serum contains both ablastin and the first trypanocidal antibody, but we removed the first trypanocidal antibody from the pooled serum by differential adsorption as described previously (*4*) to produce an "ablastic serum." Pooled serum from uninfected rats was adsorbed in the same manner and used as a control. We then could incubate immunoglobulin-free parasites in ablastic serum to produce ablastin-IgG coated cells. Control cells were of two types: those not incubated in serum in vitro and those that were incubated in adsorbed normal serum. Adult cells naturally coated with IgG were isolated from rats infected 14 days previously.

Table 2. Identification of the IgM from lactating rat serum and the second trypanocidal antibody, also an IgM, as rheumatoid factors, that is, directed against IgG coating the parasites. The numbers represent reciprocal titers as in Table 1.

Serum or serum fraction titrated	Immunoglobulin-free cells			Adult cells coated naturally with IgG
	Untreated	Coated in vitro with specific immunoglobulin by ablastic serum	Incubated in a control, adsorbed normal serum	
Lactating rat serum	0	64	0	128
IgM from late immune serum	0	32	0	32
Control serum from nonlactating uninfected rats	0	0	0	0

The results in Table 2 show that the LRSF is specific for the IgG coated cells. It is highly unlikely that this could be an anti-idiotypic IgM because the lactating rats produce the LRSF without producing ablastin (*1*). To our knowledge this is the first evidence of a rheumatoid factor helping to control an infection, although such a role was predicted (*8*).

It has been reported that IgM is not transported across rat pup intestines although LRSF apparently is (*9*). However, the evidence for IgM transport was not based on experiments with rat IgM. Recently, IgM directed against *T. musculi*, a closely related parasite specific for mice, was shown to be transferred to suckling mouse pups via milk across the pup intestine (*10*).

Since the second trypanocidal antibody, which terminates *T. lewisi* infections in nonlactating rats, is an IgM that also affects IgG-coated parasites, we considered the possibility that it too might be directed against the IgG coating the adult parasites. Table 2 shows that after isolation on Sephadex G-200, the IgM from a late immune serum (obtained 1 week after a *T. lewisi* infection was terminated) has the same specificity for IgG-coated parasites as does the rheumatoid factor in lactating rat serum. We conclude that the second trypanosomal antibody is also a rheumatoid factor, but the possibility that it is an anti-idiotype must be considered.

Although the *T. lewisi* system is useful for studying immunity to parasites, the parasite itself is of little direct importance to public health. However, a related parasite, *T. cruzi*, is the cause of Chagas' disease in South America where about 10 million people are infected (*11*). Deaths during the acute phase of *T. cruzi* infections are mostly confined to children, but chronic Chagas' disease, a fatal sequela, can develop decades after the acute phase has passed.

There are interesting parallels between *T. lewisi* and *T. cruzi* infections: (i) In both there is an acute phase with relatively high parasitemia followed by a chronic phase with reduced parasitemia (*12*); (ii) *T. cruzi* cells in mice become coated with IgG antibodies while remaining viable (*13*); (iii) lactating mice show a 50 percent survival rate when they are inoculated with a dose of *T. cruzi* that is 100 percent fatal in nonlactating female mice (*14*); (iv) a recent report showed that the titers and specificity of serum samples from mice immunized with killed *T. cruzi* are equivalent to those of serum samples from mice convalescing from infection. However, passive transfer of immunity was possible only with the convalescent serum. The author concluded that there was a factor induced by infection that was not present in the serum of animals immunized with killed parasites (*15*). We suggest that this factor may be a rheumatoid factor similar to the

second trypanocidal antibody against *T. lewisi*.

Humans and rodents may show similar rheumatoid factor responses during lactation. Rheumatoid factor occurs more commonly in women than men (*16*), and an increase in rheumatoid factor activity in humans during pregnancy or postpartum has been reported (*17*). This suggests that the ability of rheumatoid factor to enhance resistance to *T. cruzi* in rodents should be investigated and that the production of rheumatoid factor during human pregnancy and lactation should be reexamined. These results also suggest that it might be possible to treat Chagas' disease by temporarily inducing the production of rheumatoid factor. At present there are no drugs for the treatment of chronic Chagas' disease, and drugs for the acute stage are inadequate and highly toxic (*11*).

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Phase Transitions and Nonplanar Conformers in Crystalline *n*-Alkanes

Abstract. *Crystals of* n-*alkanes show a remarkable series of solid-solid phase transitions. In the odd* n-*alkanes C_{25}, C_{27}, and C_{29} a previously unknown transition is found by both calorimetry and infrared spectroscopy. The ubiquitous presence of nonplanar conformations of the chains is shown by infrared spectroscopy. The nonplanar conformers constitute approximately half the molecules in the highest temperature solid phase of C_{29}.*

The structure and phase behavior of hydrocarbon chain systems are of interest in areas as diverse as the thermal processing of synthetic polymers and the biological activity of lipid biomembranes. The high-pressure solid-solid transition of polyethylene (*1, 2*), for example, has provided a basis for understanding why cooling the polymer under high pressure leads to an unusual nonlamellar morphology (*2*). Model biomembrane systems are known to undergo two (*3, 4*) and possibly three (*5*) phase transitions in which the hydrocarbon chains play an important role. These transitions have been studied to determine their nature and biological significance (*6*).

Crystalline *n*-alkanes also undergo solid-solid phase transitions (*7, 8*) and therefore are attractive model systems. In the lowest temperature phase, the carbon skeleton of the *n*-alkane molecule is planar zigzag (all *trans*). This structural simplicity has made it possible to analyze the vibrational spectra of these molecules in great detail (*9, 10*) and to extend this analysis to include nonplanar forms (*11*). These analyses have provided the basis for interpreting the changes in the infrared spectra that we have found to accompany the solid-solid phase transitions.

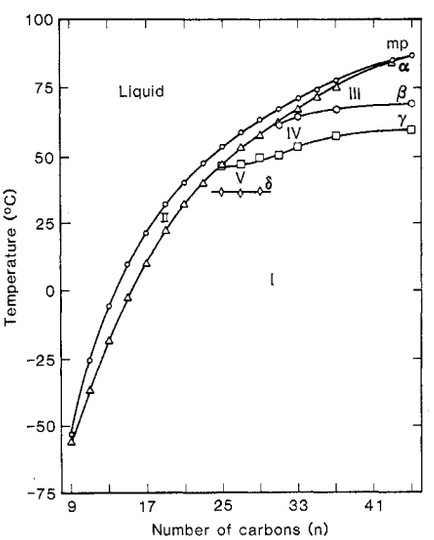

Fig. 1. Transition temperatures of odd *n*-alkanes C_n. Like transitions are connected as in a phase diagram. The solid-solid transition curves α, β, γ, and δ separate crystalline phases I, II, III, IV, and V. Transition temperatures corresponding to α, β, and γ are from (*8*), (*15*), and (*16*) and that of δ is from the present study (*17*).

We report here our observations that certain kinds of nonplanar molecules exist in crystals of *n*-alkanes and that there is a discontinuous jump in the concentration of such nonplanar molecules at each solid-solid phase transition as temperature is increased. These results were derived from infrared measurements on highly purified odd (*12*) *n*-alkanes (C_{17} through C_{29}) (*13*).

The ubiquity of nonplanar conformers is notable in that the role of conformational disorder in the high-temperature phases has not been generally recognized. Solid-solid phase transitions of *n*-alkanes have been discussed in many theoretical treatments in terms of intermolecular motion, especially rotation, of rigid planar molecules (*7, 14*). However, Strobl and co-workers (*8*) recently reported evidence for conformational defects involving *gauche* bonds in the highest temperature phase of C_{33}.

That many crystalline *n*-alkanes undergo a solid-solid phase transition a few degrees below their melting point has been known since 1932, when Müller (*7*) reported the high-temperature "hexagonal" or "rotator" phase of these systems. However, the solid phase behavior of the crystalline *n*-alkanes is complex. The situation up to about 1962 was summarized by Broadhurst (*15*) in a critical review in which the transition temperatures for the hexagonal form were tabulated. Since then, other solid-solid transitions have been reported by Strobl and co-workers (*8*) for C_{33} and by Oyama *et al.* (*16*) for C_{31}, C_{37}, and C_{45}.

Figure 1 shows transition temperatures for the odd *n*-alkanes with $n = 11$ to 45. This plot was constructed from the data cited above together with our own data from differential scanning calorimeter (DSC) measurements on C_{25}, C_{27}, and C_{29} (*17*). Our measurements revealed a new, weak transition near 37°C, which is designated δ in Fig. 1. The phases are designated I, II, and so on. Phase I is the lowest temperature phase.

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